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ANNALS of ALLERGY

PUBLISHED BY THE AMERICAN COLLEGE OF ALLERGISTS

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The American College of Allergists

First Annual Meeting

Chicago, Illinois

June 10 and 11, 1944

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March-April
1944

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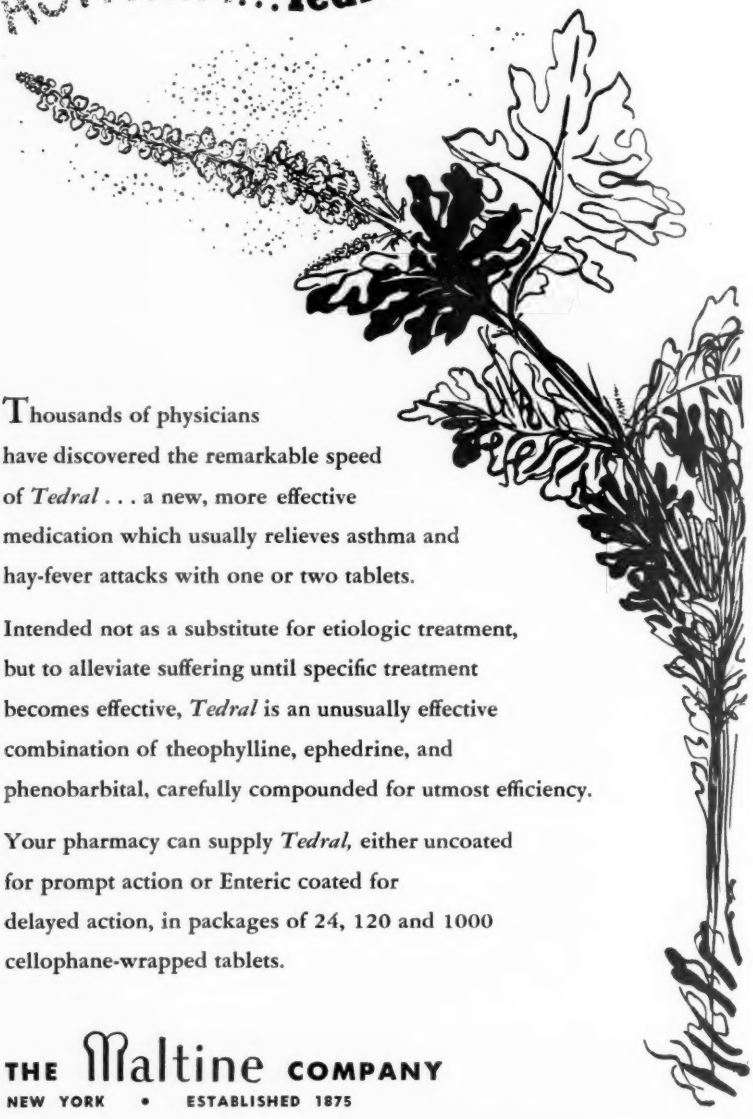

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ANNALS of ALLERGY

Published by the
American College of Allergists

Volume 2 March-April, 1944 Number 2

ALLERGIC PULMONARY CONSOLIDATIONS

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THE allergic response in the human frequently comprises symptoms referable to the respiratory tract. This response may range from a mild rhinitis to a severe reaction involving the entire pulmonary system. It seems, therefore, odd that striking pulmonary manifestations other than asthma were not recognized until Loeffler[9] reported them in 1932 and again in 1936. He described a symptom complex which he observed in patients with tuberculosis and which was characterized by the "sudden" appearance of extensive x-ray shadows in the pulmonary field. These x-ray shadows lasted at times only a few days. He stated that they resembled pneumonic infiltrations and that they were not usually accompanied by striking physical signs or symptoms. The appearance of the shadows was often related to a marked increase in the number of eosinophilic cells in the circulating blood. In one of his patients the eosinophil percentage was 66. According to his observations the symptom complex appeared almost exclusively during the summer months. Even though Loeffler first noted the condition in tuberculous patients and seemed impressed by the relationship of this syndrome of tuberculosis, only thirty-seven of his fifty-one patients were given a tuberculin test and in almost 50 per cent of these patients the tuberculin test was negative.

Since Loeffler's original description of the disease picture, many observers have reported a varying number of patients exhibiting the same clinical syndrome. The resulting picture has been often called Loeffler's syndrome or some other deceptive name. We have chosen the term allergic "consolidation" because there is no histopathological evidence to warrant the assumption that we are dealing with an inflammatory or infiltrative process. All we can say is that the pulmonary reaction leads to the formation of shadows which are recognized by roentgenograms.

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The scope of this paper does not permit a complete review of the literature which may pertain to this syndrome. We have selected a few reports which illustrate different clinical and pathological variations of this clinical complex.

In 1941 Bass[2] reported three children showing a general lymph node enlargement, leukocytosis, and extreme eosinophilia. Râles were heard throughout the chests and the breathing was described as asthmatic. In the second patient roentgenograms of the chest showed "fine pin-head shadows scattered throughout the lung." This second patient had a bone marrow biopsy which showed a white blood count of 160,000 with an eosinophil count of 20 per cent. The other two patients did not show pulmonary infiltrations. Of the three cases, two, including the one with the high bone marrow white count, recovered completely. He felt that the children did not have a truly allergic reaction but some disturbance of the blood-forming organs which simulated "eosinophilic leukemia." This report is mentioned because it emphasizes one feature of this allergic pneumonic response, namely, the extreme eosinophilia.

Wharton Smith and Alexander[11] in 1939 reported a child who showed a transitory type of pulmonary infiltration accompanied by leukocytosis and eosinophilia (39 per cent). The child was acutely ill, had a high irregular fever which was often spiking in character. However, the leukocyte count gradually fell and this was accompanied by progressive anemia. Finally, the child developed a beta hemolytic streptococcus septicemia which was heralded by a transitory leukocytosis (45,600) with 97 per cent lymphocytes) followed by a progressive leukopenia and agranulocytosis. Since the child received sulfonilamide, it is questionable whether the leukopenia was the result of this therapy. Autopsy showed a marked hyperplasia of the bone marrow but the majority of the cells were "either large or small lymphocytes and it was impossible to differentiate myeloblasts and lymphoblasts." They felt that this was an instance of fatal Loeffler's syndrome although "it seems likely that she had a leukemia." These authors, however, made a pertinent observation which will be discussed again, namely, that the "pulmonary infiltrations may occur in many conditions and may be due to various causes."

Elsom and Ingelfinger,[6] in 1942, described two patients who presented a picture of fever, pneumonitis, eosinophilia and an immune response to Brucella abortus. Both recovered and the authors felt that the disease process was a manifestation of chronic Brucellosis.

Chafee, Ross and Gunn [4] in the same year described six patients with asthma who presented a varying degree of eosinophilia and leukocytosis. All six of these patients died. It should be noted that three of them received some morphine compound. It was their impression that at least two of the patients died of pneumonia and one of them from cardiac failure. At least one of his patients developed a moderate anemia. These authors were struck by the high eosinophil count in the bone marrow material which they obtained and considered it a "very rare condition."

They also found an infiltration of the myocardium with eosinophils. It was their impression that there was nothing "to explain the amazingly high eosinophilia found in the marrow," and that "this finding of an eosinophilia in the bone marrow of asthmatic patients is unusual."

In 1943 Smith[12] reported one patient with a transitory pulmonary infiltration and emphasized the severity and chronicity of the asthmatic symptoms, transitory eosinophilia and the relatively afebrile course. He again called attention to the fact that the pulmonary x-ray shadows might be mistaken for tuberculosis, and that the prognosis might be false unless the allergic background is recognized.

During the past few years we have observed six patients with "allergic consolidation of the lung" which illustrate the various clinical features of the syndrome described first by Loeffler.

CASE REPORTS

Case 1.—A twenty-year-old white woman who had recurrent attacks of asthma for a period of twenty-one months. She developed the picture of suppurative bronchitis, x-ray evidence of a pneumonitis in the left upper lobe, leukocytosis and eosinophilia and improved after seventeen days in the hospital.

B. D. No. B 9914. This young woman was first seen July 27, 1943, because of recurrent severe asthma of twenty-one months' duration. Her father had had asthma, contracted in late adult life, for many years. Five weeks prior to admission she had her first attack of asthma and had been continuously and severaly asthmatic ever since. She had lost 20 pounds in weight. The usual remedies, such as subcutaneous adrenalin and intravenous aminophyllin, produced only slight temporary relief. Ten days prior to admission she developed a pleuritic pain in the left side of the chest; a course of sulfonamide was followed by considerable improvement. One day before admission she felt feverish and began to cough up increasing amounts of a mucopurulent sputum. Her throat became sore and her respiratory difficulty increased.

Physical examination.—Temperature 39.6° C.; pulse 100; respiration 24; blood pressure 112/76. The patient was pale, undernourished and in severe respiratory distress.

Nasal mucosa was pale, edematous and moist. Pharynx was hyperemic. There was moderate emphysema with diminished expansion bilaterally. Respirations were fast and shallow with considerable expiratory difficulty. Tactile fremitus was increased in an area around the region of the left scapula posteriorly; percussion note was dull in the right interscapular region. Numerous asthmatic wheezes were present throughout both lung fields, and there were many coarse bubbling, moist inspiratory râles at the angle of the left scapula and at the left base. Cardiac rate was rapid without other abnormalities.

Clinical findings.—Blood count is shown in Table I. Kahn and Kline tests were negative. Sputum was frothy containing a few purulent greenish-yellow masses; microscopically there were numerous gram-positive diplococci but no acid-fast organisms or fuso-spirochetes. Cultures of the sputum yielded alpha hemolytic streptococci, non-hemolytic staphylococcus albus, and citreus, a light growth of pneumococci in Avery's media; the latter couldn't be typed. Weltmann reaction was C.B. 5-½. Roentgenogram of the chest (Fig. 1) showed an area of homog-

TABLE I

DATE	W.B.C.	PER CENT EOSINOPHILS	REMARKS
7/27/43	20,950	20	Recurrent asthma—2 years. Staticus asthmaticus—5 weeks.
7/29/43	17,500	23	Physical signs and x-ray evidence of a bronchopneumonia. (Fig. 1).
7/31/43	9,850	36	On sulfadiazine—0.5 gm q 4 hr.
8/2/43	11,050	34	Afebrile after first day.
8/5/43	9,450	15	25-75 c.c. sputum daily. Sputum filled with eosinophils.
8/7/43			Skin tests to the extrinsic factors were negative.
8/13/43			Discharged—improved. (Fig. 2).
9/6/43	14,680	8	Readmitted. Asthma, chest pain and cough —3 days. Pneumonitis left lower lung. (Fig. 3).
9/9/43	12,360	12	Afebrile—sulfadiazine—0.5 gm. q.i.d.
9/14/43	16,680	21	Severe asthmatic attacks daily.
9/20/43	18,040	42	Sulfadiazine discontinued. Constant dyspnea but improved.
9/23/43	14,050 91,000 (B.M.)	40 21 (6% Myelo. E.)	Afebrile.
9/27/43	16,320	36	Still requiring symptomatic treatment daily.
9/29/43	15,880	33	
10/1/43	18,400	26	T rise to 38°C.—Sulfadiazine started again.
10/6/43	17,000	23	Severe asthma.
10/19/43	13,280	16	
10/26/43	8,720	15	Discharged—improved. (Fig. 4).
11/30/43	11,900	29	Return visit—frequent colds and occasional wheezing. Chest plate showed lung fields to be clear.

B.M.—Bone marrow obtained by sternal aspiration.
Myelo—Myelocytes.

enous clouding in the left upper lung field with a suggestion of a cavity in the upper third; also a small amount of clouding in the first interspace anteriorly on the left. Other accessory findings were negative including a tuberculin test. The clinical impression was intrinsic asthma with a superimposed bronchopneumonia.

Course in the hospital.—The patient was given sulfadiazine, 0.5 grams every four hours for ten days. The temperature fell to normal twenty-four hours after admission and remained about 37 degrees C thereafter. During the first week the patient had severe asthmatic attacks nightly, necessitating intravenous aminophyllin, subcutaneous adrenalin, aminophyllin suppositories, and tablets of ephedrine sulphate, phenobarbital and aminophyllin for relief. She expectorated 25 to 50 c.c. daily; the material was at first purulent and later clear and mucoid. Repeated examinations of the sputum showed few bacteria but many eosinophils. She was discharged after seventeen days, improved. Roentgenogram of the chest (Fig. 2) on August 12 showed that the area in the left upper lobe had decreased considerably in size. The patient was skin tested to the various pollens, contacts, foods and fungi with negative results.

She was re-admitted on September 5, approximately three weeks after discharge.

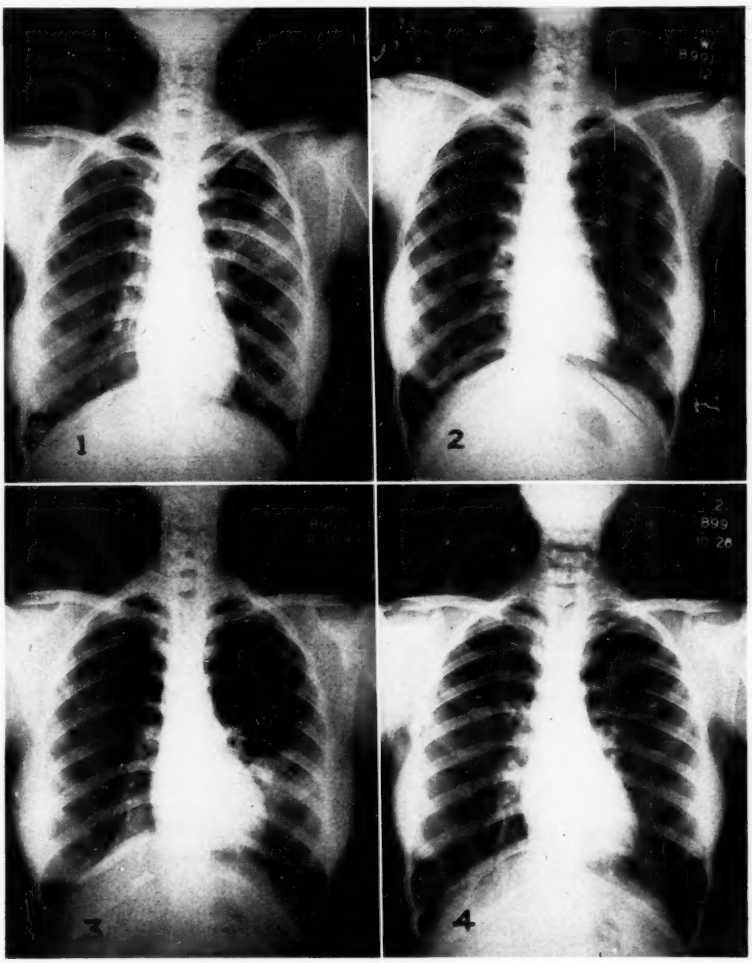


Fig. 1. (Case 1) Chest plate taken July 30, 1943, showing an area of homogenous clouding in the left upper lung field with a small amount of clouding in the first interspace anteriorly on the left. White blood count 17,500; eosinophils 23 per cent.

Fig. 2. (Case 1) Chest plate taken August 12, 1943, showing area in left upper lobe decreased considerably in size but still some residual clouding. White blood count 9,450; eosinophils 15 per cent.

Fig. 3. (Case 1) Chest plate taken September 10, 1943, showing the process in left upper lung to have completely disappeared but now an infiltration in the left lower lung field. White blood count 12,360; eosinophils 12 per cent.

Fig. 4. (Case 1) Chest plate taken October 26, 1943, showing the process in left lower lung to have largely disappeared. Both lungs are now clear. White blood count 8,720; eosinophils 15 per cent.

TABLE II

DATE	W.B.C.	PER CENT EOSINOPHILS	REMARKS
1/20/32			Asthma, intrinsic—since childhood. Chronic T & A. Skin tests negative to extrinsic factors and autogenous vaccine.
2/2/32			Marked peribronchial thickening. Suspicious of bronchiectasis.
3/27/41			Blood streaked sputum for 2 weeks. X-ray suspicious of bronchiectasis (Fig. 5).
9/2/42	39,000	80	U.R.I. Afebrile and asthma. X-ray shows patchy infiltration in right lung. Suggestive of bronchopneumonia (Fig. 6).
9/4/42	63,000	82	X-ray unchanged. Afebrile. Subjectively well.
9/8/42	52,000 79,000 (B.M.)	83 45 (9% Myelo. E.)	Skin tests were negative to the extrinsic allergens.

The asthma had returned and she complained of chest pain and cough productive of varying amounts of sputum. These symptoms had been present for three days. Temperature on admission was 38.3. Tactile fremitus was increased over the left upper chest posteriorly and both lung fields were filled with musical râles. There was a moderate tachycardia. No other physical abnormalities were evident.

Clinical Findings.—For blood counts and bone marrow studies see Table I. Roentgenogram of the chest (Fig. 3) showed the disappearance of the shadow in the left upper lung field; there was now some clouding in the left lower lung field with several suspicious areas of rarefaction. Sputum examination disclosed a large number of eosinophils, otherwise nothing of significance. The electrocardiogram showed a shift of the pacemaker to A-V node in lead 2 and a moderate sino-auricular tachycardia. The patient was given sulfadiazine, 0.5 grams four times a day for ten days. Again she became afebrile soon after admission and remained so until discharge. She had asthma almost continuously despite various remedies, including a mixture of oxygen and helium. She gradually improved and was discharged seven weeks after admission. At this time the lung fields were fairly clear by x-ray (Fig. 4). White blood count was 8,720 with 15 per cent eosinophiles.

Case 2.—A twenty-two-year-old colored man; asthmatic since childhood; x-ray shadows suggestive of bronchiectasis at both lung bases; leukocytosis with eosinophilia and severe asthma.

C. H., No. 10,718. This young colored man was first admitted in January, 1932, complaining of asthma since childhood. One brother had asthma. His history suggested the intrinsic type of asthma brought on by frequent upper respiratory infections.

Physical examination.—The patient was well nourished and adequately developed; his tonsils were enlarged and chronically infected. There was moderate emphysema. Breath sounds were accompanied by musical râles. No cardiac abnormalities were noted and the rest of the physical examination was non-contributory. A roentgenogram of the chest showed generalized peri-bronchial thickening radiating from both hila; the thickening was especially marked about the lower bronchi, "suggestive of bronchiectasis." Skin tests to the common allergens and to an autogenous vaccine were negative.

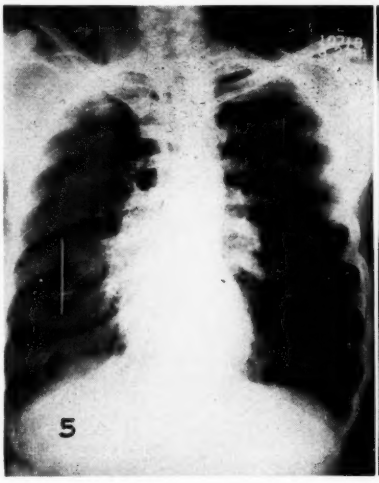


Fig. 5. (Case 2) Chest plate taken March 27, 1941, showing peribronchial thickening, especially in lower lobes suggestive of bornchiectasis.

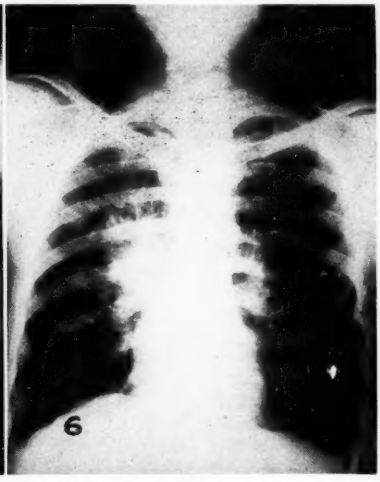


Fig. 6, (Case 2) Chest plate taken September 1, 1942, showing an increase in density around right hilum with extension upward toward the right apex suggesting a bronchopneumonia. White blood count 39,000; eosinophils 80 per cent.

In March, 1941, the patient returned complaining of a productive cough; the sputum had at times been blood streaked during the preceding two weeks. He had lost 10 pounds in weight. A week before admission the cough had become more harrassing and productive and he was expectorating about one cupful of a mucopurulent material daily.

Physical examination.—Temperature, pulse and respiration were normal. There was no evidence of sinus infection. The pharynx was reddened, and tonsils were enlarged. Musical râles were heard throughout the chest and moist inspiratory râles in both hilar regions. Heart was normal. Blood pressure was 114/80. Roentgenogram of the chest (Fig. 5) showed an increase in the peri-bronchial thickening in both lower lobes and some thickening of the right interlobar fissure. There were no tubercle bacilli or spirochetes in the sputum. The patient returned September 1, 1942, because of a recurrence of the asthma following an upper respiratory infection. Examination disclosed that the breath sounds were increased over the left anterior chest; there were moist and crepitant râles over the right lower chest anteriorly and the left lower chest posteriorly.

Clinical Findings.—White blood count was 39,000 with 80 per cent eosinophils (Table II). A chest plate showed a considerable increase in density around the right hilum extending towards the apex "suggesting a bronchopneumonia." There was a marked peri-bronchial thickening in both lung fields consistent with bronchiectasis (Fig. 6). Weltmann reaction was C.B. 5. Kahn and Kline tests were negative. The patient returned one week later feeling better. Skin tests to the various allergens including fungi were negative. Cultures of the sputum yielded pharyngis siccus, alpha hemolytic streptococcus, and anaërobic bacteria. Complete blood and bone marrow studies were done at this time (Table II).

TABLE III

DATE	W.B.C.	PER CENT EOSINOPHILS	REMARKS
10/15/40	16,500	51	Asthma—3 years. Athlete's foot—2 months. X-ray shows thickening around hila (Fig. 7). Severe dermatophytosis. Bilat. Caldwell-Luc and ethmoidectomy. Started desensitization. Afebrile.
10/18/40	22,050	19	
9/17/42	6,750	8	Recurrence of asthma following a cold.
1/21/43	24,000	8	Staticus asthmaticus—1 week. Mottled consolidation in both mid lungs (Fig. 8).
1/27/43	17,800	35	Severe asthma. Chest filled with coarse and fine moist rales.
1/29/43	21,000	16	Staticus asmaticus continues.
2/8/43	22,000	24	Improving.
2/11/43	28,000	39	
2/16/43	13,000	59	Chest clear. Asymptomatic
2/17/43	11,000 121,000 (B.M.)	47 7 (17% Myelo. E.)	Discharged.
4/9/43	6,800 53,000 (B.M.)	18 5	Return visit. Greatly improved. Chest plate taken (Fig. 9).

Case 3.—A thirty-five-year-old white woman who gave a history of asthma of four years' duration and a negative family history for allergy. In the fourth year of her asthma she developed severe bronchospasm and x-ray signs of consolidation in both mid-lungs accompanied by leukocytosis and eosinophilia without fever.

J. W. No. A 49242. This patient was first seen October 15, 1940, giving a history of asthma of four years' duration. Family history was negative for allergy. Asthmatic symptoms were preceded by recurrent nasal obstruction, sneezing and rhinorrhea, the first attack of asthma occurring one year later, soon after an operation on the nose. The nasal symptoms were most pronounced in the spring and fall, whereas the asthma was usually precipitated by upper respiratory infections.

Physical examination.—The patient was well developed and nourished, but coughed and wheezed considerably. She had moderate seborrhea and acne of the face, shoulders, and trunk. Nasal mucosa was pale, and there was no nasal discharge. The right antrum was cloudy. Tonsils were hyperemic and ragged. There was slight emphysema. Constant inspiratory musical râles could be heard throughout and coarse inspiratory râles at the left base. Heart was normal. The rest of the physical examination was non-contributory except for moderate dermatophytosis about the left great toe.

Clinical findings.—Hemoglobin and red blood count were normal. White blood count was 15,500 with 51 per cent eosinophils (Table III). Kahn and Kline tests were negative. Roentgenogram of the sinuses showed densely thickened membranes of the antra and ethmoids. Roentgenogram of the chest showd bronchial thickening about both hila, particularly on the left side, and deformity of both diaphragms (Fig. 7). Sputum culture yielded alpha streptococci, staphyloccus aureus, and anaërobic bacteria. Skin tests to common allergens gave positive reactions to dust, a few pollens and molds. The clinical impression was a mixed type of asthma and chronic maxillary sinusitis. The patient entered the hospital and had a bilateral Caldwell Luc and ethmoidectomy. After discharge she was given a series of autogenous vaccine treatments with marked improvement.

She returned two years later because of a recurrence of severe asthma, having

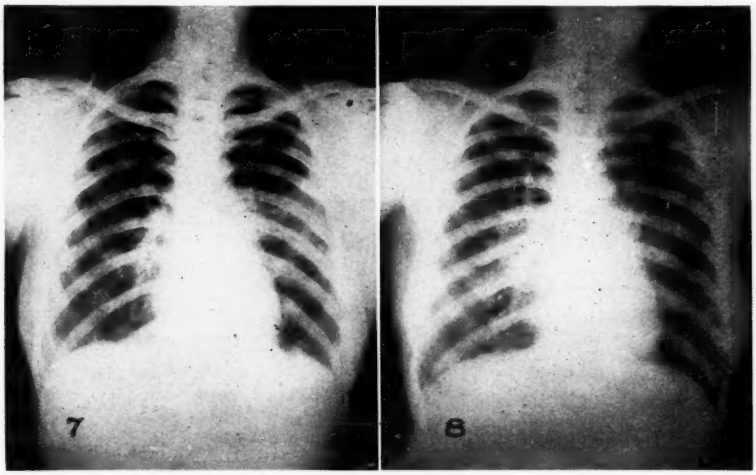


Fig. 7. (Case 3) Chest plate taken October 15, 1940, showing generalized peribronchial thickening at both hila, especially the left. Diaphragms are deformed by adhesions. White blood count 16,500; eosinophils 51 per cent.

Fig. 8 (Case 3) Chest plate taken February 10, 1943, showing mottled consolidation in both mid lungs. White blood count 28,000; eosinophils 39 per cent.

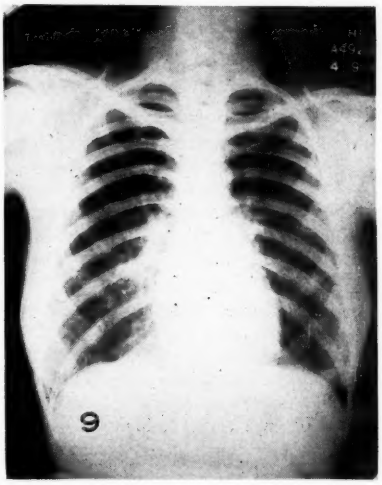


Fig. 9. (Case 3) Chest plate taken April 9, 1943, showing bronchial thickening in the lower lobes but no definite infiltration. White blood count 6,800; eosinophils 18 per cent.

stopped her autogenous vaccine treatments in the fall of 1941 soon after the birth of her baby. She had got along very well until two weeks before re-admission when she developed a fresh upper respiratory infection. This was accompanied by severe paroxysmal cough, productive of whitish mucus and severe nocturnal asthma.

TABLE IV

DATE	W.B.C.	PER CENT EOSINOPHILS	REMARKS
8/15/42	66,000	59	Asthma—3 weeks. Numerous musical rales. X-ray shows increased hilar markings. (Fig. 10).
8/25/42	56,560 120,700 (B.M.)	71 42 (9% Myelo. E.)	Feeling well. Skin tests to extrinsic allergens were negative. Low-grade fever. 37.5°C.
9/14/43	57,000	69	Report from L.M.D. Child passed round worm.
10/20/43	64,000 142,400 (B.M.)	64 33	Marked thickening around right hilum. Soft infiltration in lung field suggestive of tbc. Asymptomatic except for nocturnal cough. (Fig. 11).
4/6/43	19,000 110,000 (B.M.)	24 14 (2% Myelo. E.)	Looking well, feeling well. Some cough. Has been dewormed.
7/6/43	10,450 74,000 (B.M.)	14 15 (3% Myelo. E.)	(Fig. 12). Asymptomatic. Examination essentially negative.

The important physical findings were inspiratory and expiratory musical râles throughout both lung fields.

Clinical findings.—Hemoglobin and red blood count were within normal limits; white blood count normal; eosinophils 8 per cent. Roentgenogram of the chest showed essentially the same findings previously described. Skin tests gave mild positive reactions to giant and short ragweed, river birch, white oak, dogwood, box elder, dust, orris root and rabbit epidermis. The patient was again started on autogenous vaccine treatments. She returned three months later because of severe asthma. At this time the chest was filled with asthmatic râles.

White blood count was 24,000, eosinophiles 8 per cent. The chest plate disclosed a mottled consolidation throughout both lung fields (Fig. 8). The clinical impression was that she had asthma with superimposed bronchopneumonia, probably of virus origin.

Sputum culture revealed alpha hemolytic streptococci, diphtheroids, N. siccus and anaërobic bacteria. No tubercle bacilli or pneumococci were obtained. The patient was skin-tested to all of the vaccines prepared from these organisms with negative results. Weltmann reaction was C. B. 4. She had a persistent tachycardia and severe asthma for a period of two weeks, refractory to the usual methods of treatment. She was given sulfadiazine without definite improvement. Bone marrow studies were done (Table III). She improved gradually and was discharged after thirty-two days in the hospital. Roentgenogram of the chest at this time showed a decrease in the consolidation in the left mid lung. The patient returned April 9, 1943, feeling quite well. Roentgenogram of the chest at this time disclosed bronchial thickening in the lower lobe but nothing to suggest tuberculosis. "A diffuse process with this clearing might suggest sarcoid" (Fig. 9. The white count was normal but the eosinophilia persisted. A tuberculin test was negative.

Case 4.—A one-year-old white boy with asthma of three weeks' duration, showing a marked leukocytosis and eosinophilia. Roentgenogram of the chest showed increased peri-hilar markings without infiltration (Fig. 10). Practically afebrile course.

B. H. No. A 89851. This boy was admitted to the hospital August 8, 1942, with asthma of three weeks' duration. The grandparents were asthmatic. Two weeks before admission the child developed a slight fever without signs of a marked

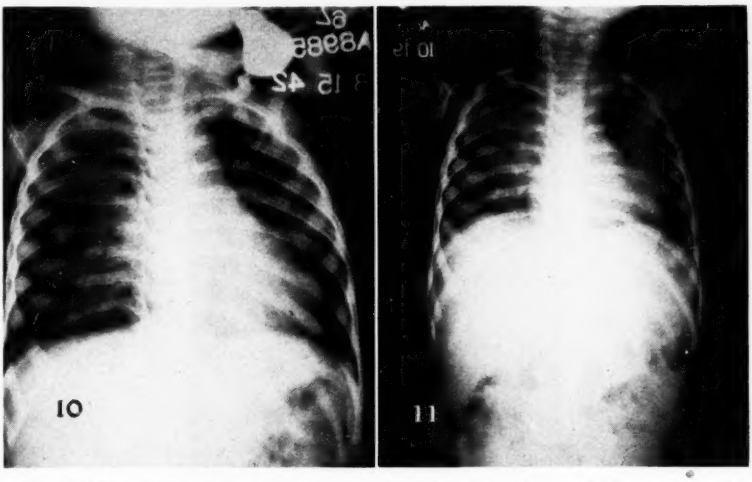


Fig. 10 (Case 4) Chest plate taken August 15, 1942, showing increased hilar markings but no definite infiltration. White blood count 66,000; eosinophils 59 per cent.

Fig. 11. (Case 4) Chest plate taken October 19, 1942, showing marked thickening around the right hilum with some parenchymal infiltration of the soft variety suggestive of tuberculosis. White blood count 64,000; eosinophils 64 per cent.

upper respiratory infection. He was given a purgative and very soon thereafter he had considerable difficulty in breathing and audible wheezing. On the fourth day he had a severe attack of bronchospasm. The family physician diagnosed pneumonia, and the child was hospitalized for four days. He improved during the next two weeks but three days before admission the respiratory difficulty returned, accompanied by a harsh dry cough.

Physical examination.—Well developed and nourished. Tonsils moderately enlarged and reddened; anterior cervical lymph nodes palpable. Numerous musical rales throughout both lung fields; no moist rales. The remainder of the examination non-contributory.

Clinical findings.—Hemoglobin 9 gms. (58 per cent), white blood count 66,000 with 59 per cent eosinophils (Table IV). A chest plate showed increased hilar markings without infiltration (Fig. 10). The child was sent home and got along very well. He returned ten days later for reëxamination. At this time roentgenogram of the chest was essentially as previously noted. Examination of the chest showed nothing abnormal. However, the white blood count was 56,560 with 71 per cent eosinophils. (Blood smears obtained from three siblings and patient's father were studied: one brother had an eosinophilia of 5 per cent without leukocytosis.) The question of eosinophilic leukemia was raised and bone marrow studies were done (Table IV). At this time skin tests to the common allergens were negative. Weltmann reaction was C. B. 2. Sputum and gastric washings failed to show tubercle bacilli. Schick and tuberculin tests were negative. Stool examinations were noncontributory. The patient was given 120 c.c. of citrated blood without reaction. He was discharged five days after admission apparently feeling well.

He returned two months later for a recheck. In the interim he had had three fairly severe attacks of asthma and a persistent nocturnal cough. According to his mother, he had passed two round worms two weeks previously. On examination

he had a papulo-pustular skin rash over the chest and buttocks. There were occasional coarse inspiratory bronchi at the right base after coughing. Spleen was palpable 3 cm. below the costal margin. Complete blood and bone marrow studies were done (Table IV). Roentgenogram of the chest showed marked thickening

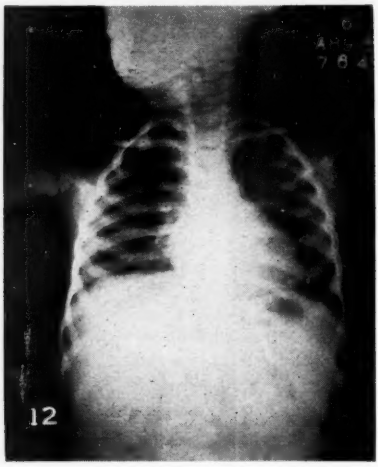


Fig. 12. (Case 4) Chest plate taken July 6, 1943, showing decrease in the amount of peribronchial infiltration on the right. White blood count 10,450; eosinophils 14 per cent.

around the right hilum with a soft parenchymal infiltration. "The appearance is suggestive of tuberculosis" (Fig. 11). He gave a 2 plus reaction to the intradermal injection of 0.1 c.c. of a 1:100 dilution of ascaris antigen. Six months later the child returned for reëxamination. In the meantime he had been dewormed, and repeated stool examinations were negative for ova and parasites. He had been quite well, except for occasional nocturnal coughing. On examination a few moist inspiratory rales were heard at the left base. The spleen was still palpable. Blood and bone marrow studies were repeated (Table IV). Another roentgenogram of the chest showed a decrease in the amount of peribronchial infiltration on the right side and no evidence of recent localized infiltration (Fig. 12). Weltmann reaction was C. B. 5. He returned three months later feeling quite well. The physical examination was entirely non-contributory. The spleen was no longer palpable. White blood count was 10,450 and the eosinophils 14 per cent.

Case 5.—A twenty-nine-year-old white woman with a history of asthma of about one years' duration following an acute upper respiratory infection. Roentgenograms of the chest showed a mottled consolidation throughout both lung fields. Moderate leukocytosis and eosinophilia, palpable spleen, afebrile course.

M. D. No. A 56322. This young white single woman was first seen in this hospital February 17, 1941, complaining of frontal and generalized headaches of two months' duration. Nothing was found to account for these headaches. Roentgenograms of the skull and sinuses gave negative findings. There was no family history of allergy. The patient returned two years later in status asthmaticus. Three months previously she had what she called "pneumonia" which was followed within a few

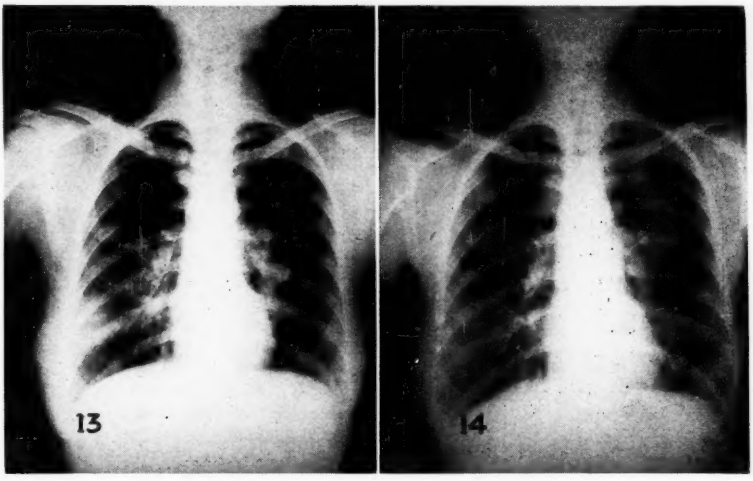


Fig. 13. (Case 5) Chest plate taken June 3, 1943, showing patchy consolidation throughout the mid portions of both lung fields. White blood count 10,050; eosinophils 18 per cent.

Fig. 14. (Case 5) Chest plate taken July 12, 1943, showing some clearing on the right but still considerable consolidation. White blood count 15,350; eosinophils 47 per cent.

TABLE V

DATE	W.B.C.	PER CENT EOSINOPHILS	REMARKS
2/17/41			P.H. Exertional dyspnea—2 years. Bitemporal headaches—3 months. Blurred discs.
5/31/43	27,000	1	Pneumonia 3 months previously. Recurrent asthma. Staticus asthmaticus. Bronchopneumonia by x-ray. Sulfadiazine started.
6/2/43	10,050	18	(Fig. 13).
6/10/43	20,400	23	
6/12/43	17,600 63,000 (B.M.)	25 27 (5% Myelo. E.)	X-ray therapy to lungs.
6/14/43	20,000	25	
6/17/43	16,350	19	
6/21/43	14,200	60	Asthmatic.
6/22/43	19,550	52	
6/28/43 7/2/43	20,000 25,500	46 40	
7/5/43	13,900	46	Asthma continues.
7/8/43	22,200	43	
7/12/43	15,350	47	(Fig. 14).
7/16/43	16,600	43	Discharged. Still some asthma.

weeks by recurrent attacks of bronchospasm of gradually increasing frequency and severity.

Physical examination.—The patient was acutely ill, in severe respiratory distress, moderately cyanotic, with slight papilledema. Tonsils were large and injected.

TABLE VI

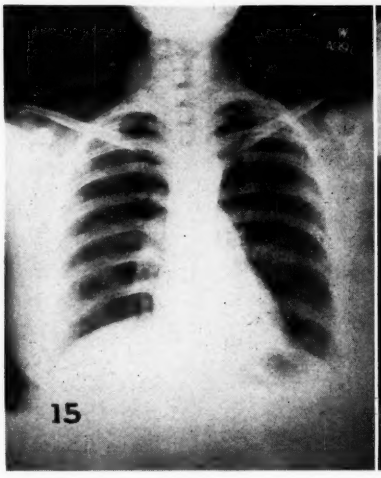
DATE	W.B.C.	PER CENT EOSINOPHILS	REMARKS
2/1/43	20,600	0	Hospitalized. Acute tracheobronchitis. Asthmatic wheezes throughout chest. Chest plate negative. (Fig. 15). Fever subsided 2 days after sulfadiazine was started.
11/12/43	10,250	8	Cough and some wheezing irregularly for the past 10 months. Contracted an U.R.I. one previously and asthmatic since.
12/7/43	8,900	30	Readmitted. Recurrence of tracheobronchitis. Coughing and wheezing. Afebrile. Scattered inspiratory musical and coarse rales throughout chest. No moist rales. Chest plate showed clouding in right upper lobe suspicious of tbc. (Fig. 16).
12/10/43	10,600	34	On sulfamerazine. Improved.
12/11/43	11,400 47,880 (B.M.)	35 9 (4% Myelo. E.)	Afebrile—less asthma.
12/13/43	14,150	29	
12/14/43	8,100	50	Chest clear by x-ray. (Fig. 17).
12/16/43	8,950	29	Discharged
1/10/44	7,800	15	Asymptomatic. Lungs clear by x-ray and on physical examination.

There was moderate emphysema; marked tachypnoea (48 per minute). The chest was full of musical rales with diminished breath sounds at the right base. The spleen was palpable.

Clinical findings.—White blood count was 27,000; eosinophils 1 per cent (See Table V). The clinical impression was asthma and early broncho-pneumonia. Roentgenogram of the chest showed a patchy consolidation throughout the mid portions of both lungs (Fig. 13). Kahn and Kline tests were negative. No acid-fast organisms or fusospirochetes were found in the sputum. Culture of the sputum gave N. catarrhalis, N. siccus, and anaërobic bacteria. Skin tests were inconclusive with slight positive reactions to the intradermal injections of giant and short ragweed, dust and few molds. Immunological studies for Brucella were negative. Electrocardiogram was normal. Weltmann reaction ranged between C. B. 4 and C. B. 6. The patient had severe asthma for more than six weeks which did not respond to the usual remedies including oxygen and helium. The patient was afebrile throughout. Soon after admission she developed an eosinophilia and this, as well as the leukocytosis, persisted throughout her hospital stay. She was also given pertussis vaccine as well as a series of x-ray treatments to the lungs without benefit. Repeated roentgenograms of the chest were made and all showed mottled consolidation throughout both lung fields. The last chest plate on July 12, 1943, still showed considerable consolidation but some clearing of the process (Fig. 14). The white blood count was still elevated, but the patient was symptomatically improved.

Case 6.—A thirty-year-old married white woman complained of asthma of one month's duration; family and past personal histories negative for allergic disorders. Severe attack initiated by upper respiratory infection. Leukocytosis and moderate eosinophilia. Intractable asthma. X-ray picture of consolidation of right upper lobe with cavitation; afebrile course.

S. K. No. A99019. This patient was admitted on January 30, 1943, complaining of asthma of one month's duration. One month previously she had contracted an



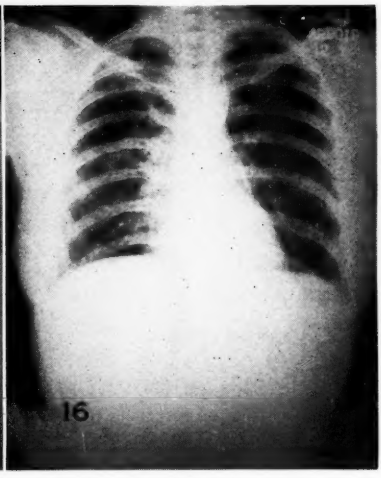


Fig. 15. (Case 6) Chest plate taken February 1, 1943, showing lungs to be essentially clear. White blood count 20,600; eosinophils 0.

Fig. 16. (Case 6) Chest plate taken December 7, 1943, showing a diffuse infiltration in the right upper lobe with a suspicious cavity near the right hilum. The appearance is suggestive of tuberculosis. White blood count 8,900; eosinophils 30 per cent.

upper respiratory infection and the cough and malaise persisted until admission. She expectorated moderate amounts of a mucopurulent material. Four days before admission she had her first attack of bronchospasm; the respiratory distress increased and only temporary relief was afforded by subcutaneous adrenalin.

Physical examination.—The patient was well developed, moderately obese, asthmatic, coughing frequently and perspiring freely. The nasal mucosa was hyperemic with a moderate mucopurulent discharge. The paranasal sinuses were clear on transillumination. Pharynx was dry and hyperemic. Limited equilateral expansion of the chest. Tachypnoea (32 per minute). Scattered inspiratory, expiratory musical râles throughout both lung fields. No moist râles heard. Heart rate 112 per minute. No other abnormalities noted.

Clinical findings.—Hemoglobin was 15 gms. (97 per cent), red blood count 5,000,000, white blood count 20,600 (Table VI). Kahn and Kline tests were negative. There was a trace of albumin in the urine. Roentgenogram of the chest showed no abnormalities. (Figure 15). Sputum culture yielded alpha hemolytic streptococci, staphylococcus albus, N. siccus, hemolytic diphtheroids and anaerobic bacteria. Stool examination was negative.

The patient was afebrile on admission, but on the second hospital day the temperature went to 38.6° C. She was now given sulfadiazine, 1 gm. four times daily and this was continued for five days. The temperature fell to normal on the third day and ranged around 37° thereafter. Her asthma responded to oral ephedrine sulphate with phenobarbital and aminophyllin, and aminophyllin suppositories. She was discharged on the eighth hospital day markedly improved. She returned six months later because of a recurrence of asthma. In the interim she had had an occasional cough and substernal tightness. Following a cold spell of weather the cough became productive of mucopurulent material. She felt that she had contracted an upper respiratory infection, and at this time began to wheeze. Examination in the clinic showed that she was in moderate respiratory distress. Tempera-

ture was normal, pulse 100, respirations 20, blood pressure 120/88. Skin was flushed and moist. Nasal mucosa and pharynx were hyperemic. Numerous musical râles, inspiratory and expiratory, were heard throughout both lung fields. A few

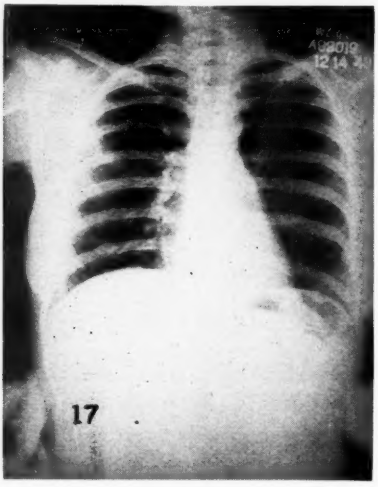


Fig. 17. (Case 6) Chest plate taken December 14, 1943, showing the previous infiltration to have largely disappeared. White blood count 8,100; eosinophils 50 per cent.

moist inspiratory râles were heard after coughing at the lung bases. Complete blood studies were done (Table VI). The patient was instructed to remain in bed, force fluids and to use the remedies previously prescribed. Skin tests done at this time showed slight positive reactions to the intradermal injections of giant and short ragweed, Jersey pine, pussy willow, pecan, chrysanthemum, daisy fleabane, dust, goat epidermis, rice, coffee, alternaria, and oidomycin. Cultures from her sputum yielded alpha hemolytic streptococci, staphylococcus aureus, N. catarrhalis, N. siccus, and a mixture of anaërobic bacteria. An autogenous vaccine was prepared from these organisms which was combined with the allergens mentioned and desensitizing treatments were started. She got along very nicely until the latter part of November when she developed an acute attack of asthma which did not respond to the remedies which had previously proved effective. She was readmitted to the hospital December 5, 1942, in a status asthmaticus.

Physical examination.—The patient was acutely uncomfortable, coughing and expectorating considerable amounts of thick yellow material. The chest was filled with inspiratory, musical and coarse râles; no moist râles were heard and there were no expiratory noises. Temperature was normal.

Clinical findings.—Hemoglobin was 16.1 gms. (90 per cent), red blood count 5,150,000, white blood count 8,900 (Table VI). Weltmann reaction was C.B. 2-½. Urine was normal. Brucella agglutinations gave negative findings. Roentgenograms of the sinuses revealed no abnormalities. Stereoscopic views of the chest showed a diffuse infiltration in the right upper lobe with a "suspicious" cavity near the right hilum. The appearance was suggestive of tuberculosis (Fig. 16). The electrocardiogram was normal except for tachycardia and inverted T 1. The patient remained afebrile throughout her hospital stay of twelve days. On the second

hospital day she was given sulfamerazine, 0.5 gm. every four hours, and this was continued for one week. The usual remedies were employed to insure symptomatic relief of her asthma. She was relatively free of asthma during the last three days of her hospital stay. A chest plate repeated on December 14, 1943, showed that the infiltration in the right upper lobe had largely disappeared (Fig. 17). She returned for observation on January 10, 1944, stating that she had felt perfectly well since discharge from the hospital. White blood count was 7,800 with eosinophils 15 per cent. Roentgenogram of the chest showed the lungs to be clear.

DISCUSSION

The syndrome of allergic pulmonary consolidation is featured therefore by: (1) varying degrees of pulmonary consolidation, at times multiple, often migratory, and recognized by roentgenographic examination of the chest; (2) its occurrence in allergic individuals; (3) a varying leukocytosis and eosinophilia; (4) an afebrile clinical course; (5) persistent, severe asthma; (6) lack of response to the known sulfon drugs; (7) history of frequent upper respiratory infections.

Pathogenesis.—We have detailed the histories of six patients, who presented evidences of a pulmonary infiltrative reaction, with slight or no fever, accompanied by a marked eosinophilic leukocytosis of bone marrow origin. The sputum contained many eosinophils. Since no postmortem studies have been made of lungs showing the above type of reaction, its exact nature is unknown, but it is well established that mesenchymal and endothelial tissues can become sensitized, and react in an allergic manner, on subsequent contact with an offending allergen. Why certain individuals show an eosinophilic, pneumonia-like reaction, while others do not, is not readily explicable, but since this type of tissue reaction is encountered mostly in allergic individuals it would seem that the constitutionally hypersensitive person has some tissue peculiarity which results in this type of response.

Although some allergists still doubt the existence of an allergic response to bacteria, the immunological studies of Finland,[7] his co-workers and others, as well as clinical experience, have provided evidence that the tissues can become sensitized to bacterial products, whether they be protein or carbohydrate in nature. Several years ago, one of us[1] reported a number of clinical examples which showed that the skin will develop, in some individuals, an allergic response to various bacteria if sensitized by B. erysipelatis. It was demonstrated that subsequent erysipeloid reactions could be provoked by a number of bacteria which had no close immunological relationship to the sensitizing beta hemolytic streptococcus of erysipelas. There is no reason why a similar condition should not obtain in the bronchial tree, i.e., a susceptible individual becomes sensitized to one or a group of bacteria, or their products, in the course of repeated upper respiratory tract infections, and then shows an allergic response of the pneumonic type of reaction to a re-infection with the sensitizing, or some other type of bacterial antigen. All six of our patients gave a history of frequent upper respiratory tract infections.

Harkavy,[8] in a series of recently published studies, has reëmphasized the importance of the vascular system in allergic reactions and has described the various vascular alterations which may accompany the allergic phenomena. Undoubtedly, many of the clinical manifestations of hypersensitiveness are colored by symptoms of vascular origin, and it is generally accepted that the fundamental allergic response is due to disturbances in the vascular system. These disturbances may range from a simple transitory exudation and edema, with or without a perivascular cellular response, to irreversible vascular changes which result in the death of tissues. In many instances, such an injury to the vascular system is accompanied by a striking eosinophilia. This has been demonstrated by the studies of Rich[10] which he describes in his article on periarteritis nodosa. Describing a series of animal experiments, he states "these experiments demonstrate that periarteritis nodosa is one manifestation of the anaphylactic type of hypersensitivity." Careful study of patients with periarteritis nodosa will demonstrate the parallelism between this syndrome and the more severe forms of recognized allergic disturbances."

Eosinophilia.—The cause of the eosinophilia remains unknown. Whether it is a response to increased mobilization of histamine, as has been suggested, or to increased need for this substance, supposedly carried by eosinophils, has not been shown. All we can say definitely is that eosinophilia is of bone marrow origin and is part of the general allergic response (Figs. 18 and 19). The degree of eosinophilia does not indicate the severity of the allergic reaction, but marked eosinophilia often accompanies the clinically more severe allergic manifestation.

Chillingworth[5] and co-workers reported experiments on dogs in which they produced temporary emphysema by insertion of an intratracheal ball-valve. All their animals developed leukocytosis promptly and, in many instances, marked eosinophilia. They concluded that the eosinophilia is "reflex" and is caused by expiratory delay with overdistention of the alveoli. Adrenalin did not modify these eosinophilias. In the same paper, however, they described the effect of adrenalin on two asthmatic patients with eosinophilia and one patient with chronic eczema and eosinophilia. The degree of eosinophilia was reduced materially twenty-four hours after the administration of adrenalin in the asthmatic patients but not in the patient with eczema. The leukocyte count and the eosinophil count were followed carefully over the twenty-four-hour period; no changes in the degree of eosinophilia were observed within one hour after adrenalin administration. This is at variance with the previously reported observations of Camp[3] who maintained that the eosinophils are markedly increased within one hour by adrenalin dosage. We have tried the effect of adrenalin on three of our patients with allergic consolidation and have observed the absence of response as described by Chillingworth. However, we disagree that the eosinophilia of the asthmatic is purely a reflex phenomenon but believe that it is an expression of the allergic state. Certainly, it is

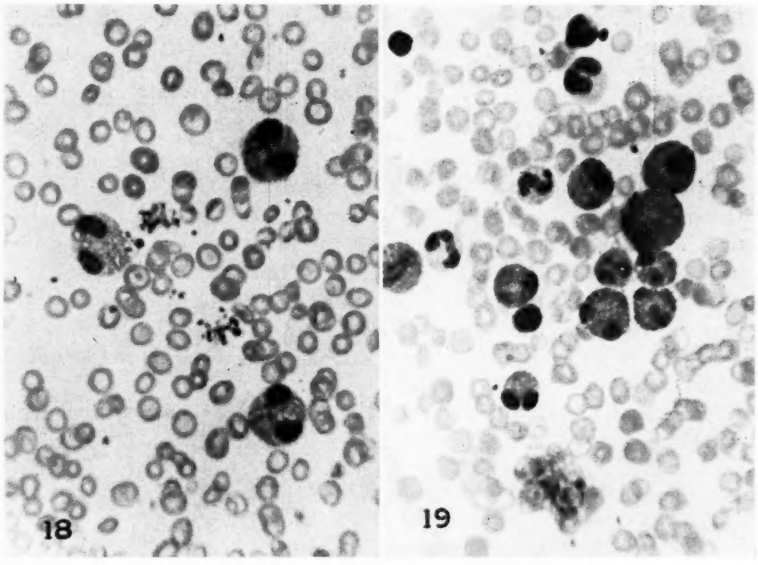


Fig. 18. (Case 3) Eosinophils in peripheral blood.

Fig. 19. (Case 3) Eosinophils in bone marrow.

well known that the eosinophilia of asthmatic individuals persists after the cessation of bronchospasm and in the absence of evidence of alveolar overdistention. The sweeping conclusions of Chillingworth furthermore disregard the marked eosinophilia which often is found in nonasthmatic allergic individuals suffering from atopic rhinitis, eczema and other expressions of allergy. Thomas and Taylor,[13] in a recent article on allergic bronchitis, noted a moderate degree of eosinophilia in over half of their patients; they concluded that a persistent eosinophilia was usually the rule in those who responded poorly to treatment and that it could, therefore, be considered a sign of poor prognosis.

As far as we could determine, the incidence of allergic consolidation of the lung was not an indication of an exceedingly sypersensitive individual, although we realize that methods of evaluating the degree of hypersensitiveness in the human are still very inadequate. The degree of skin reactivity to test allergens was certainly not greater in our group of patients with allergic pneumonic reactions than in a comparable group of other allergic subjects; if anything, it was less. It is quite possible that the degree of eosinophilia marks the severity of vascular injury. This is suggested by the occurrence of eosinophilia in such conditions as periarteritis nodosa and Hodgkin's disease. In any event, the eosinophilia is of myeloid origin, a generalized systemic phenomenon and not, as has been previously thought, confined to or initiated by the pulmonary tissue.

Moreover, as illustrated by our sixth patient, a persistent eosinophilia is compatible with complete symptomatic recovery.

Diagnosis.—The diagnosis of allergic pulmonary infiltration should offer no difficulty if the patient is carefully studied. The roentgenological findings are varied and by themselves, may prove confusing. In our group of patients the pulmonary involvement suggested either bronchiectasis or bronchopneumonia, or tuberculosis or sarcoid. The differentiation of allergic pneumonic infiltration from *bacterial pneumonitis* (bronchopneumonia, bronchiectasis with pneumonitis) is based on the absence of fever, or severe intoxication and the character of the sputum. The usual polymorphonuclear cell response, without any appreciable eosinophilia, will feature the bacterial type of pneumonitis, which so frequently responds to the sulfon drugs.

In *virus pneumonia* there is, as a rule, a paucity of physical signs with variable x-ray evidence of pulmonary consolidation, but the leukocyte count is normal or decreased and again eosinophilia is lacking. *Ascariasis* may conceivably simulate the circumstances which obtain in an allergic pneumonia. One of our patients (Case 4) was found to be infected with ascaris; however, the disease picture persisted after he was dewormed. Naturally, the stools should be carefully searched for ova and parasites in every instance of eosinophilia.

The x-ray picture of pulmonary and mediastinal *sarcoid* is notoriously variable; since the process is often quite indolent, it may suggest an allergic pneumonitis if it occurs in an asthmatic patient. In two of our patients (Cases 2 and 3) the sarcoid was suggested by the x-ray picture. The correct diagnosis of sarcoid is based upon the x-ray finding of other abnormalities such as cystic areas in the terminal phalanges, hyperproteinemia and the frequently demonstrable skin lesions and lymph node involvement. Eosinophilia of any marked degree is infrequent in sarcoid.

The x-ray picture of the chest in allergic pneumonic infiltration often suggests *pulmonary tuberculosis,* particularly if the process is confined to one or the other of the upper lobes of the lung. In two of our patients (Cases 1 and 6) pulmonary tuberculosis was the initial roentgenological diagnosis. The examination of the sputum which shows numerous eosinophils in the sputum of a patient with allergic pneumonic response, the presence or absence of tubercle bacilli, elastic fibers, Curschmann's spirals and the history, the clinical course and the peripheral leukocytes response should lead to the correct diagnosis.

Treatment.—Severe asthma, often of long duration, was in all our patients the outstanding presenting symptom. The same is true of the majority of the cases of a similar type of pneumonic reaction reported in the literature. Our group of patients proved relatively refractory to the usual forms of treatment, including the prolonged use of oxygen, helium and mixtures of these two gases. Several patients were treated empirically by

the administration of pertussis vaccine without benefit. Refractory asthma in a patient with a marked eosinophilia should always suggest the possibility of an allergic pneumonic infiltration and, if cloudy areas can be demonstrated by x-rays, usually it means that the patient's asthma will respond more slowly to the common remedies than does uncomplicated status asthmaticus. Heroic measures are not indicated in such patients and often prove quite disappointing. Because of the prolonged asthmatic seizures, patients with an allergic infiltration of the lungs, particularly in private practice, are given morphine or some similar alkaloid. This is definitely contraindicated, since these drugs produce a contraction of smooth muscle and accentuate the bronchospasm.

Sulfa drugs are useful if there are evidences of a bacterial infection, such as a purulent bronchitis, naso-pharyngitis, or sinusitis, but have no effect on the allergic pneumonic process. We wish to warn against the indiscriminate use of the sulfon drugs in allergic patients, particularly those with an allergic pneumonic infiltration. Aminophyllin by mouth, in combination with ephedrine sulphate and phenobarbital (100 mgm., 15 mgm., respectively), every four hours, and rectal installations of aminophyllin (500 mgm. in 60 c.c. of water), or suppositories of aminophyllin (250 mgm.) have proven quite helpful in relieving the asthmatic distress in most of our pateints. The therapeutic response was much slower in this group than in the usual asthmatic. We have rarely used adrenalin since the above-named medications always produced sufficient relief to insure some rest to the patient. Intravenous aminophyllin was rested to only in very ill patients when there were no detectable evidences of myocardial embarrassment. All the patients were given salt water enemas daily as long as they were severely asthmatic. Fluids were forced and fruit juices were given in large amounts. In addition, every patient received a mild sedative by mouth or rectally once or twice a day, to allay anxiety and induce restful sleep.

SUMMARY

The syndrome first described by Loeffler consists of migratory pulmonary reactions occurring as a rule in allergic individuals, accompanied by leukocytosis and a varying degree of eosinophilia. In view of the fact that the exact nature of the pulmonary reaction remains obscure, and since we cannot state whether it consists of an infiltration or an inflammatory reaction, we believe that the term allergic pulmonary consolidation is acceptable, because it does not indicate a specific histopathological change.

The pulmonary changes are usually discovered by x-ray examination of the chest; the usual physical signs of intra-pulmonary change are masked by the auscultatory signs of bronchospasm. A concomitant severe and often intractable asthma is the rule.

The eosinophilia in our six patients is obviously of myeloid origin and persists in a moderate degree after the disappearance of asthma and of the x-ray evidences of pulmonary consolidation.

Our six patients who developed allergic pulmonary consolidation gave a history of repeated upper respiratory infections and the acute episode appears to have been precipitated by a fresh infection in the respiratory tract. Sulfon drugs wre efficacious in controlling the acute infection; they are indicated in patients who have purulent sputum. Once the acute infection responds to the sulfon drugs, the clinical course becomes afebrile regardless of the extent and persistence of pulmonary consolidations, leukocytosis or eosinophilia.

Individuals who develop allergic pulmonary consolidation are always severely asthmatic. The asthma tends to persist until the pulmonary consolidation clears considerably or disappears; allergic pulmonary consolidation should be suspected in all individuals with intractable asthma and marked eosinophilia and leukocytosis. Furthermore, it will undoubtedly prove worth while to examine the peripheral blood of patients with intractable asthma; if leukocytosis and eosinophilia are found, roentgenograms of the chest should be taken to demonstrate or rule out the presence of pulmonary consolidation as the cause of the therapeutic failure.

The pulmonary x-ray shadows seen in allergic consolidation are quite variable, and may be mistaken for pulmonary sarcoid, virus pneumonia, tuberculosis and pyogenic pneumonitis.

We believe that allergic pulmonary consolidation is an expression of sensitization to nonspecific bacteria and that it can occur in constitutionally allergic individuals as well as in individuals who acquire the allergic response.

Allergic pulmonary consolidation is often a very severe syndrome which may last for weeks, but so far fatalities have not been observed.

The treatment of allergic consolidation of the lungs is the treatment of the presenting symptom of asthma. Sulfon drugs have no effect on the duration or extent of pulmonary consolidations nor on the degree of leukocytosis or eosinophilia.

SUMARIO

El sindrome primeramente descrito por Loeffler, consiste de reacciones pulmonares fugaces que por regla general ocurren en individuos alérgicos, acompañadas por leucocitosis y un grado variable de eosinofilia. En vista del hecho de que la exacta naturaleza de la reacción pulmonar permanece obscura y desde que no podemos establecer si consiste en una infiltración o en una reacción inflamatoria, creemos que el término Consolidación Alérgica Pulmonar es aceptable porque ello no indica un cambio histopatológico específico.

Los cambios pulmonares son generalmente descubiertos por medio de radiografías. Los datos auscultatorios y de exploración habituales se encuentran enmascarados por los signos auscultatorios del broncospasmo. Generalmente se encuentra acompañado de asma intenso y a menudo de mal asmático.

La eosinofilia en nuestros seis pacientes es evidentemente de origen

mieloide y persiste en un grado moderado despues de la desaparición del asma y de los hallazgos radiográficos.

Nuestros seis pacientes que desorrollaron consolidación alérgica pulmonar presentaron una historia de repetidas infecciones del árbol respiratorio superior y el episodio agudo parece haber sido precipitado por una nueva infección del tracto respiratorio. Las Sulfa drogas fueron eficaces para controlar la infección aguda; son indicadas en pacientes que tienen esputo purulento. Una vez que la infección aguda responde a las Sulfa drogas, el curso clínico se vuelve sin fiebre sin importar del grado y persistencia de la consolidación pulmonar, leucocitosis o eosinofilia.

Los individuos que desarrollan consolidación alérgica pulmonar son siempre severamente asmáticos. El asma tiende a persistir hasta que la consolidación pulmonar alérgica se disipa considerablemente o desaparece; consolidación pulmonar debe sospecharse en todos los individuos en status asmáticus y marcada eosinofilia y leucositosis. Además debe hacerse un hemograma de los pacientes con asma rebelde; si se encuentran leucocitosis y eosinofilia se debe sacar radiografía del pecho para demostrar o excluir la presencia de consolidación pulmonar como la causa del fracaso terapéutico.

Las sombras radiográficas pulmonares son completamente variables y pueden ser confundidas con una neoplasia, neumonia a virus, tuberculosis y neumonitis piógena.

Creemos que consolidación alérgica pulmonar es una expresión de sensibilización no-específica bacteriana y que ello puede ocurrir tanto en individuos de constitución alérgica como en individuos que se hacen alérgicos.

Este es un sindrome intenso que puede durar varias semanas, pero hasta ahora no han sido observados casos de muerte.

El tratamiento de consolidación alérgica de los pulmones es el mismo usado para el asma. Las Sulfa drogas no tienen efecto sobre la duración o extensión de la consolidación pulmonar ni sobre el grado de leucocitosis o eosinofilia.

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PROSTIGMIN TREATMENT OF PERIODIC HEADACHES

L. Pelner and M. E. Aibel (J. Lab. & Clin. Med., 1942, 27:1546) have added to Horton's group of vascular headaches, those headaches skin sensitive to acetylcholine as well as to histamine. They report a new method of treatment based on this theory. The authors studied a series of sixty patients with periodic headaches, migraine and histamine cephalalgias. All patients in this group were skin sensitive to histamine and/or acetylcholine.

Based on the action of prostigmin in liberating and preserving acetylcholine, the authors thought that repeated acetylcholine "shocks" produced by small increasing doses of prostigmin might produce a desensitization of the patient to acetylcholine in the same manner as histamine cephalalgias are desensitized to histamine by Horton's technique. The procedure is as follows: A solution consisting of one 15-mg. tablet of prostigmin bromide, dissolved in one ounce of water, is administered in doses of one drop three times a day, progressively increasing each dose by one drop until 30 drops are reached. Then 30 drops were given each day for one week, and thereafter every other day until the patient was free from symptoms for a reasonable length of time.

The skin reaction in 40 per cent of the patients tested decreased with desensitization treatment with prostigmin. The acetylcholine wheal and flare were always reduced in size after treatment. All of the periodic headaches, whether of the histamine type described by Horton, or migrainous, were relieved definitely to a great extent.

Pelner (Dis. Nervous System, 1943, 4:177) further reports the results obtained in treating forty-six patients with periodic occipital headache by this method of treatment. Hypersensitivity to acetylcholine or histamine on skin testing was demonstrated in all. In all except three of the cases, the occipital headaches were considered to be vascular in origin, caused by an accumulation of metabolites causing vasodilatation.

SKIN REACTIONS TO PATCH TEST WITH HUMAN DANDER

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IN a previous report evidence was presented demonstrating the existence of an allergen in human dander, human hair from the scalp, and seborrhoeic eczema scales.[3] The allergen was not detected in epidermis from the general body surface, hair from the scalp of a newborn infant, or in hair and other contents of a dermoid cyst of the ovary. The presence of the allergen was demonstrated by means of skin reactions. These were obtained in certain patients with atopic eczema when the tests were performed by the *scratch* method. *Intradermal* tests in passively sensitized skin sites were positive, thus demonstrating the presence of reagins. *Patch* tests were not performed on any of these patients. Later, however, it was decided to do tests by this method on some of the same and on other patients.

EXPERIMENTS

Materials and Methods.—Human dander (dandruff) from the scalps of normal adults was obtained by the use of clean fine combs. The dander was mixed with just sufficient petrolatum to make a thick paste, a thin layer of which was spread on a small piece of blotting paper and applied directly to the skin as a patch test. The patches were allowed to remain in position for two days. Readings were made at the time of removal of the patch, fifteen minutes later and in some cases on the following day and one week later.

For scratch tests the dander was rendered oil-free by ether extraction. It was then extracted in 50 per cent glycerine, the volume of glycerine used being approximately five times that of the loosely packed dander. The extract was passed through a Seitz filter and used undiluted for scratch tests directly on patients. For intradermal tests in passively sensitized skin sites 1-100 carbolized buffered saline dilutions of this extract were used. Tests were performed on:

1. Twelve children with eczema. These were routine office admissions, not selected cases.
2. Nine patients with atopic eczema, aged twelve to twenty-six years.
3. Twelve atopic children and adults without atopic eczema.
4. Twenty-five nonatopic children and adults including eight newborn infants.

The criteria for the diagnosis of atopic eczema were the presence of typical clinical lesions, positive skin reactions to foods or inhalants (scratch method), positive family history of atopy and, in some cases, the presence of other manifestations of atopy in the patient.

From the Departments of Medicine and of Bacteriology and Immunology of the University of Louisville School of Medicine.

TABLE I. SKIN REACTIONS TO HUMAN DANDER

Case No.	Age	Clinical Diagnosis	Patch Test	Scratch Test	Passive Transfer
1	5 mos.	Eczema*	–	–	–
2	12 mos.	Eczema*	++	–	–
3	12 mos.	Eczema*	++	–	–
4	16 mos.	Eczema*	++	–	–
5	17 mos.	Eczema*	+++	–	–
6	20 mos.	Eczema*	+++	–	–
7	20 mos.	Eczema*	–	–	–
8	2 yrs.	Eczema*	–	–	–
9	3 yrs.	Eczema*	+++	–	–
10	5 yrs.	Eczema*	–	–	–
11	5 yrs.	Eczema*	++	–	–
12	5 yrs.	Eczema*	++	–	–
13	11 yrs.	Atopic eczema	–	–	–
14	12 yrs.	Atopic eczema	–	+++	+++
15	17 yrs.	Atopic eczema	–	++	++
16	17 yrs.	Atopic eczema	–	+++	+++
17	19 yrs.	Atopic eczema	–	+++	+++
18	21 yrs.	Atopic eczema	–	+++	++
19	22 yrs.	Atopic eczema	–	++	++
20	22 yrs.	Atopic eczema	–	++	++
21	26 yrs.	Atopic eczema	–	–	–
22	3 mos.	Asthma	–	–	
23	21 mos.	Asthma	–	–	
24	3 yrs.	Asthma	–	–	
25	6 yrs.	Asthma	–	–	
26	6 yrs.	Asthma	–	–	
27	8 yrs.	Asthma	–	–	
28	12 yrs.	Hay fever	–	–	
29	25 yrs.	Hay fever	–	–	

Results.—A positive reaction to patch test was manifested by an area of redness, slight swelling and numerous fine, superficial elevations at the site of application of the dander. This reaction was seen a few minutes after removal of the patch and also on the following day. Seven days later a slightly scaly eczematous patch was clearly visible. Nine positive reactions were obtained to patch tests (Table I). With one exception these occurred in young children with eczema; of twelve such cases, eight gave positive reactions. The exception was that of a four-year-old child without clinical manifestations of atopy. His mother, however, had childhood eczema and his mother's sister has asthma. It is interesting to note that while the older children and adults with atopic eczema gave negative reactions to patch tests with human dander, in seven of nine cases eleven

Case No.	Age	Clinical Diagnosis	Patch Test	Scratch Test	Passive Transfer
30	27 yrs.	Hay fever	–	–	
31	30 yrs.	Hay fever	–	–	
32	40 yrs.	Hay fever	–	–	
33	49 yrs.	Hay fever	–	–	
34	Newborn	Nonatopic	–	–	
35	Newborn	Nonatopic	–	–	
36	Newborn	Nonatopic	–	–	
37	Newborn	Nonatopic	–	–	
38	Newborn	Nonatopic	–	–	
39	Newborn	Nonatopic	–	–	
40	Newborn	Nonatopic	–	–	
41	Newborn	Nonatopic	–	–	
42	2 yrs.	Nonatopic	–	–	
43	2 yrs.	Nonatopic	–	–	
44	2 yrs.	Nonatopic	–	–	
45	3 yrs.	Nonatopic	–	–	
46	3 yrs.	Nonatopic	–	–	
47	4 yrs.	Nonatopic	–	–	
48	4 yrs.	Nonatopic	++	–	–
49	4 yrs.	Nonatopic	–	–	
50	5 yrs.	Nonatopic	–	–	
51	5 yrs.	Nonatopic	–	–	
52	7 yrs.	Nonatopic	–	–	
53	9 yrs.	Nonatopic	–	–	
54	35 yrs.	Nonatopic	–	–	
55	38 yrs.	Nonatopic	–	–	
56	40 yrs.	Nonatopic	–	–	
57	44 yrs.	Nonatopic	–	–	
58	47 yrs.	Nonatopic	–	–	

*For information regarding type of eczema refer to Table II.

years of age or older there were positive reactions by the scratch method and in all of these reagins were demonstrated by local passive transfer. Reactions to patch and scratch tests on the control subjects, with the one exception noted above, were negative (Table I).

An analysis of cases Nos. 1 to 12 is given in Table II.

DISCUSSION

The etiologic significance of positive reactions to patch tests with human dander in children with eczema appears to be worthy of investigation. All children undoubtedly have daily contact with human dander, either from their own scalp or from that of parents, nurse or other attendants.

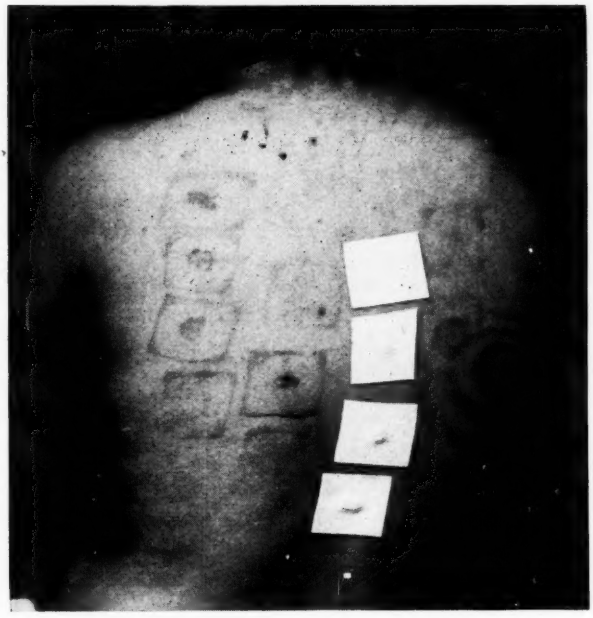
TABLE II. ANALYSIS OF THE TWELVE CASES OF INFANTILE AND CHILDHOOD ECZEMA

Case No.	Age	Character of lesions	Location of lesions	Scratch tests to foods and inhalants	Family History of atopy	Patch test to human dander	Scratch test to human dander
1	5 mo.	Papular circumscribed Erythematous	Upper and lower extremities, face	Egg ++++	+	−	−
2	12 mo.	Papular Erythematous Diffuse, scaly	Face Arms Forearms Legs	−	+	++	−
3	12 mo.	Erythematous Diffuse Scaly	Face Forearms Legs Thighs	Egg +++	+	++	−
4	16 mo.	Papular, scaly Diffuse and circumscribed	Upper and lower extremities. Popliteal spaces. Thumb	−	+	++	−
5	17 mo.	Diffuse, scaly on face. papular and erythematous	Face. Cubital spaces. Legs Thighs	Egg ++++	+	+++	−
6	20 mo.	Erythematous Diffuse Scaly	Face Wrists Cubital spaces	−	+	+++	−
7	20 mo.	Erythematous circumscribed Patchy areas	Thighs only	−	±	−	−
8	2 yrs.	Erythematous circumscribed and diffuse	Arms. Forearms Popliteal spaces Behind ears	−	+	−	−
9	3 yrs.	Diffuse Scaly	Right cupital space. Right wrist. Right forearm	−	−	+++	−
10	5 yrs.	Erythematous circumscribed	Face. Cubital and popliteal spaces	−	±	−	−
11	5 yrs.	Diffuse Scaly	Face. Arms Forearms Popliteal spaces	−	+	++	−
12	5 yrs.	Erythematous Scaly Diffuse	Face. Forearms Cubital spaces Thighs. Legs	Wheat ++	+	++	−

If human dander should actually prove to be an important causative factor in infantile and childhood eczema, the fact would explain several perplexing problems. For example, it would account for the fact that the disease is not present at birth but often begins several weeks or months later, after a period of time required for exposure and development of hypersensitiveness. In some cases this condition develops while the child is still nursing the breast and before it has received any food other than mother's milk. Allergy to human dander would account for the occurrence of the disease in certain cases in which all skin tests performed with foods and inhalants are negative. It would also explain the frequent failure of food elimination to result in healing of the lesion.

While the hypothesis offers explanations for several hitherto unexplained facts, it also poses several questions. Is this reaction an atopic

response of the epidermis or is it a reaction of the superficial layer of the corium, due to "transepidermal penetration"?[4] Is it possible that this contact reaction to human dander represents the so-called "seborrhoeic element"[2] of infantile eczema and that this element is in reality an allergic,



REACTIONS TO TESTS WITH HUMAN DANDER

First row (on the left): Positive reactions to three different specimens of dander from normal adult scalps. Negative reaction to "cradle cap" from an infant, aged three months.

Second row: Negative reaction to patient's own eczema scales. Positive reaction to patient's own dander from scalp. Negative reaction to wool.

Third row: Four patches in position.

Fourth row: Tests done seven days before photograph was taken showing one strong reaction still clearly visible.

probably atopic, response to surface contact with human dander having its source chiefly in the scalps (and secondarily on clothing, et cetera) of parents and others, possibly even the child himself? Do children sometimes "outgrow" their eczema because they get too large and too heavy to be held comfortably by their mothers? Why do the lesions occur on the face, neck, and flexures of the arms and legs much more frequently than on the scalp? Why does the skin, in a significant proportion of cases, improve greatly or clear up entirely in hot weather? Is the allergen present also in the lesions? What is its biologic origin? Is it cornified epidermis? Or does it have its origin in some microörganism? These and other questions can be answered only by further study.

It must be emphasized that no one allergenic excitant will account for

all cases of atopic eczema, a disease in which multiple sensitivity is the rule. In fact, some cases (a rather small percentage, however) may be explained on the basis of food allergy. Attention is called to the fact that the type of response to patch test described herein is not unique but appears to be identical with that described by Albert and Walzer,[1] obtained with silk, feathers, et cetera, in atopic children; not exclusively, however, in patients with atopic eczema.

SUMMARY

A skin reaction to patch test with human dander is described. The reaction was elicited in eight of twelve children with eczema and in one child without eczema. Other children without eczema gave negative reactions. Adults with and without atopic eczema gave negative reactions to patch tests but seven of nine persons, eleven years of age or older, with atopic eczema gave positive reactions to scratch test with human dander. In all of the latter, reagins were demonstrated by passive transfer.

It is suggested that the etiologic significance of these reactions to patch test with human dander is worthy of investigation.

SUMARIO

Se ha descrito una reacción cutánea a la prueba de "patch" con caspa o epitelio de seres humanos.

La reacción fué descubierta en 8 de los niños con eczema y en un niño sin eczema. Otros niños sin eczema dieron reacciones negativas.

Adultos con o sin eczema atópico dieron reacciones negativas a la prueba de "patch," pero 7 de 9 individuos, de edad de 11 años o más, con eczema atópico, dieron reacciones positivas al método de escarificación con caspa. En todos los últimos casos, la existencia de reaginas fué demostrada por el método indirecto o de trasporte pasivo.

Se hace la sugestión que la significación etiológica de estas reacciones a la prueba de "patch" con caspa de seres humanos vale ser investigada.

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FOOD ALLERGY

The Role of Food Allergy in Internal Medicine

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FOOD allergy is a problem which concerns every physician in the practice of medicine. While it is not necessary that every doctor be able to make a complete diagnosis of food sensitization, it is important that he be sufficiently informed on the subject that he may correctly evaluate it in the differential diagnosis. He should also be able to advise the patient concerning the nature of the procedures necessary to the evaluation of this problem.

This paper is based upon more than a score thousand deliberate feeding tests and the subsequent follow-ups made during the past twelve years. It is hoped that at least part of the information obtained from this study will be an aid to the physician not specializing in allergy, in the evaluation of food sensitization.

DEFINITION

Food allergy, in this communication, refers to those foods which, under correct conditions of testing, produce definite clinical manifestations. These reactions must be not only constant with repeated trial, but also must exhibit specificity. Thus, for example, one is considered allergic to a food if it (a) increases his blood pressure; (b) produces ulnar neuritis; or, (c) induces asthma or hay fever. This restricted definition excludes foods which give skin reactions and foods suspected of causing symptoms, but which, in either instance, cannot be proved by deliberate test.

INCIDENCE OF FOOD ALLERGY

Vaughan[1] has indicated that about 60 per cent of the general population is subject to food allergy, of which 50 per cent is considered minor, not a medical problem, and 10 per cent is major, requiring medical attention.

The incidence of food allergy in patients with common allergic syndromes may vary from only one sensitization in the more fortunate allergic, to practically every food used regularly by the patient. Contrary to general opinion, the number of foods to which one becomes sensitive increases with age—adults having more food allergies than children. In hay fever the average is about five foods, in perennial nasal allergy it is nearer seven, while in asthma it is above ten per patient. This is what would be expected since the frequency of use of a given food is a major factor in precipitating an allergy to it. There are several other conditions which

Presented before the Southwest Allergy Forum, Fort Worth, Texas, May, 1941. Presented as a symposium on Food at the Fourth, Fifth and Sixth Annual Forums on Allergy. Read February 22, 1944, at the Doctors' Dinner Club, Oklahoma City, Oklahoma.

influence the development of food allergies. These are infections, particularly measles, whooping cough and especially influenza. These four precipitating causes of sensitization are: frequency of feeding, measles, whooping cough and influenza. They are, however, dependent upon another factor which I have called "the inherent tolerance for foods."

Patients vary greatly in their ability to eat the same food repeatedly before becoming sensitive to it. This tolerance, in turn, predicates the eventual degree of relief that these patients will obtain, other factors being correctly treated. The severity of symptoms in the untreated patient is not a guide to the degree of food tolerance. The percentage of compatible foods among those used almost daily, however, is a reliable indication of this inherent tolerance. It is important to determine early in the treatment of a patient as to whether his tolerance for foods is high or low. If it is true that the patient has become sensitive to 70 per cent of the foods used daily, it is to be expected that he will also become sensitive to many of those substituted for foods eliminated because of sensitivity. This fact formulates the real criticism of the elimination diet, namely—any patient who is so ill that one must use a diet of three or four foods to analyze his food allergies, is too ill to be kept on such a diet. It has been proved on many occasions that a week's constant use of a food will induce an active allergic state and that the use of the restricted diet often increases the patient's total number of allergies.

CLINICAL CONDITIONS DUE TO FOOD ALLERGY

Where does one expect to find food allergy? Obviously it is a factor in asthma and perennial nasal allergy and, to a lesser extent, in seasonal hay fever. It is also a common cause of headaches, hives and infantile eczema. These are the common allergic syndromes in which food allergy occurs more or less constantly, but there are a great number of other clinical syndromes in which food sensitizations are of import. These are: arthritis, sciatica, lumbar pain, ulnar neuritis, insomnia, hypertension, toxemia, tachycardia, anginal attacks, nervousness and general irritability as well as bladder irritation, hematuria, albuminuria and vertigo.

The variety of conditions in which foods have been found to be a factor naturally prompts the question as to what criteria one may use as a guide for initiating studies for food allergies. What are the indicators that food sensitization may be the cause of a given set of symptoms? It is not the failure to find any other explanation for the condition, but rather the presence of several definite facts which may be determined partly by history and more fully by observations.

CRITERIA INDICATING FOOD SENSITIZATION

If certain symptoms could be due to foods and no organic cause has been found, these criteria will be a useful guide providing at least two of the three points exist in a given case.

1. The patient, from time to time, will have itching of the nose or the

naso-pharynx. If this is denied upon history taking, have observations made over a period of time. This sign is seldom absent in food allergy.

2. At various times the patient will retire free of symptoms and either be awakened out of sleep with an attack of asthma or nasal allergy or develop such upon arising. Again he may be subject to the constant daily level of symptoms and awaken from sleep with a definite exacerbation or have a flare immediately upon arising.

3. There should be exacerbations of typical symptoms which last two to three days. These may be either superimposed upon constant symptoms, or may develop and continue in a patient otherwise symptom-free.

While there are patients in whom food sensitizations occur in which not one of these three criteria are present, nevertheless, these are reliable guides to warrant dietary studies. These criteria are dependent on the fact that practically every allergic individual is sensitive to foods that are used intermittently and will, therefore, produce exacerbations.

VALUE OF SKIN TESTING

Every informed physician today knows that skin testing for foods is not entirely reliable, whereas testing for inhalants is of exceptionally high value. One will find in large groups of patients that at least 20 per cent of the foods actually the cause of allergic symptoms will give skin reactions, while a positive test is associated with clinical reaction after ingestion of the food about 40 per cent of time. There is no evidence to indicate that frequent skin testing and retesting with food extracts will do other than to add to the general confusion.

It may be stated without fear of successful contradiction, that one should not stop using skin tests, neither should they be used unless they are supported by immediate and definite diagnostic programs in connection with such tests. Vaughan[2] covered this subject with consummate finality when he stated, "Skin tests represent a point of departure in the therapeutic program."

The basis of all other diagnostic measures is the demonstration of a specific allergic reaction by deliberate ingestion of the food. Since October, 1932, I have completed over a score thousand of individual feeding tests. It is my opinion, based upon this experience, that the most valuable fact in the diagnosis of food allergy is a knowledge of its nature and mechanism of reaction. Further, this information should be visualized so that it may be applied in clinical practice.

THE NATURE OF FOOD ALLERGY

Food allergy may be classified as being either (1) fixed—(constant sensitization), or (2) cyclic—(intermittent sensitization). The fixed food allergy is one that is not affected by the frequency of the food in the diet. Even if one has not eaten the food for many years, the first ingestion of it is followed by definite, often violent, symptoms.

The cyclic food allergies are those that become clinically evident with

the use of the food and tend to disappear with omission of the food. In other words, the presence or absence of an allergic status is determined by the incidence of the food in the diet. The course of such an allergy, briefly, is as follows:

If one uses a food every day or so, he may be allergic to it but never suspect it as a cause of symptoms. It is common to feel better after the

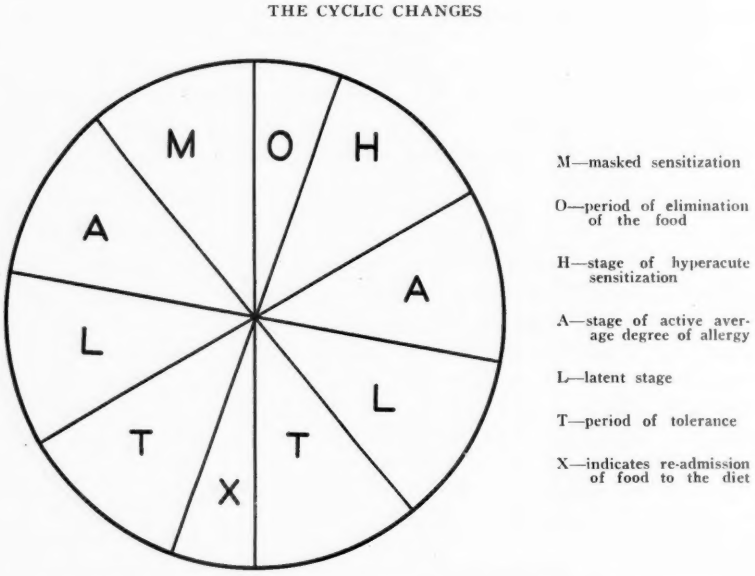


Fig. 1. In this diagrammatic outline of the changes in food allergy, time is conceived as going clockwise. The circle is broken down into three phases, each of which has several important subdivisions.

meal at which this food is used, than before mealtime. This is called a masked food allergy. When the food is eliminated long enough that all symptoms due to its last ingestion have ceased and it is eaten again, it may—and often does—produce increased and sometimes severe symptoms which occur shortly after the meal. If the food is thereafter continuously avoided except for tests, these changes will occur. First, there will be an active but decreased clinical reaction, after which there develops a latent type of sensitization. In this latter state, symptoms are not observed if the food is eaten, for example, on Tuesday, but then do occur following the use of the same food on Friday or Saturday of that same week. With further avoidance, one gains tolerance to the food. If, at that time, it is readmitted to the diet and used with definite regularity, these stages of sensitization will recur—first the latent and then the active state of sen-

sitization. Should the food be used frequently it will become a masked food allergy.

Thus, one has completed a cycle of responses to the same food, these variations being mediated by either the omission or use of the food.

Cyclic food allergy is of three clinical types:

1. *The perennial.*—This is a primary food allergy.

2. *The concomitant.*—This is a food allergy, clinically evident only while one inhales an allergen—for instance, ragweed. It is highly specific.

3. *The thermal.*—These are of two types, the first being a sensitization that is clinically evident, but very mild in warm weather. It becomes of paramount importance when the patient breathes cold air, or otherwise approximates the chilling effect of the inhalation of cold air. The second type of thermal sensitization does not evidence itself until the patient is exposed to cold air or is chilled at, or below, his critical level.

I wish to emphasize that the idea of changes in food sensitization is not new as many allergists have reported and published diagrammatic outlines of such changes. Our visualization of the subject is slightly different and seem to fit in with clinical factors very well.

Phase I. Changing Response to Foods.—This stage is the period of time in which the effect of foods change from masked or non-suspected allergens, to reactors associated with immediate and often hyperacute symptoms following ingestion. It consists of several closely related sequences of events.

(a) In the first period of this phase, called the masked stage, the patient will be repeating the food in the diet before the symptoms, produced by the previous ingestion, have entirely subsided.

(b) The second feature is the omission of the food until all symptoms produced by the previous ingestion have subsided.

(c) The final period of this phase is the reintroduction of the food into the diet at the end of period "b" above.

The clinical importance of this phase may be summed up as follows:

1. The first and most important fact is that neither the patient nor the physician can tell, with certainty, if a patient is allergic to a food that is used under conditions which will allow masking of reactions.

2. Except for fixed food allergies, all the hyperacute and severe reactions, all the definite exacerbations of symptoms that affect patients for three to five days at a time, which are due to foods at all, are due to foods in which either by accident or deliberate intention, the successive steps of Phase I have taken place. Reactions from foods having masked reactions, will vary all the way from mild definite symptoms to collapse in ten min-

utes after ingestion, when previously the patient may have felt better after its use.

3. Since these reactions normally last three days in warm weather and may continue five days in winter, one will be on the alert for multiple causes if symptoms do not subside in due course of time.

4. The occurrence of hyperacute reactions or definite flares at once suggests an intermittent cause of such reaction. This fact prompts one to search for this type of reactor.

5. It can be seen that it is important to know not only what a patient eats, but also how he eats. Such information can be obtained only from a dietary record.

6. One can never accept any patient's or physician's statement based upon history and skin tests only, that certain foods either do, or do not, cause allergic reactions.

7. Because of masked allergies, there is often confusion on the part of the patient as to the causative factors. It is the rule that if the patient thinks nearly all foods bother him, he is senstive to one common food that is obtained in many foods. The best example of this is corn. Conversely, if he reports that no matter what he eats he has about the same amount of trouble, it is very apt to be due to a common food used daily.

8. The complaint of the patient with masked allergies and his actual symptoms are not the same. He states he has trouble as soon as he arises, again around 10:00 to 11:00 A. M., again about 4:30 and around 9:00 to 10:00 P.M., and if the degree of allergy is great enough, in the middle of each night. Actually, in addition he has short, mild flares after each meal.

9. A patient not knowing the facts detailed here, may make changes in how he eats that will result in severe symptoms, although he has not changed the actual foods used. You may deliberately make these same changes for diagnostic purposes.

10. You may expect symptoms ranging all the way from a mild itching of the nose to collapse within ten minutes after ingestion in patients who test foods in the final period of Phase I.

Phase II. Decreasing Degree of Sensitization.—The three periods of this phase are—the period of active sensitization, which in turn is followed by that of latent sensitization and, this, in turn, by tolerance for the food. These three periods are not abruptly and sharply defined but fuse into one another to make these changes progressive and less spectacular than the changes which occur in Phase I. The active stage of sensitization is simply less in degree, but all reactions are definite and quite immediate. When the latent state is reached, immediate symptoms are very mild, and one must observe for flares during the night or the next morning, to detect reactors.

Tolerance for a food may be assumed when no demonstrable symptoms can be produced by its ingestion. It is a relative, not absolute tolerance.

The clinical significance of this phase may be summed up as follows:

1. It may take as little as twelve days to as much as two years to pass through the three periods of Phase II.

2. It is very difficult to determine with finality the effect of foods in the latter part of this phase. Any commitments made to the patient should be made with due regard to these facts.

3. Single feeding tests are not of themselves a sufficient means of diagnosis in the latent sensitizations.

4. When patients have had foods removed from their diets following deliberate feeding tests, they should not have these foods replaced without taking into consideration the changes which have resulted from omission and the changes which will occur in the third phase of the cycle.

Phase III. Increasing Degree of Sensitization.—If, when the patient has acquired tolerance for a food, it is replaced in the diet and used as it was before the diagnosis of allergy was made, the sensitization will recur. The latent reactions come first, then active sensitization returns so that after each ingestion symptoms occur. If the frequency of the food in the diet is three or four times weekly, the stage of masked allergy will be produced. These are the important clinical features of this phase:

1. The change from tolerance to active sensitization may occur within one week.

2. If a food is added when the patient tolerates it, and it is kept in the diet continuously, masked symptoms may be produced without the patient or physician suspecting it as a cause of reaction.

Symptoms which begin insidiously and gradually increase, are typical of foods added to the diet in this period of the cycle.

3. Foods used at intervals of seventy-two hours may mask their symptoms.

4. It is not correct to tell a patient, who has been off a food for months or more, to go home and eat a lot of it and see if it produces symptoms.

5. When patients are seen who have been off foods for a long enough time to have gained a tolerance for the food, do not destroy this tolerance. Evaluate all the factors concerned before issuing instructions for the use of such foods. It is as important to a patient to have his tolerance for a food preserved as it was for him to know originally that a given food was a cause of symptoms.

CLINICAL APPLICATION OF THE CYCLIC CONCEPT

The value of the cyclic concept is only in that it helps one to visualize the dynamic changing nature of food sensitization. It is important to realize the rapidity of the changes in all three phases, but particularly in that of the decreasing and increasing degrees of sensitization (Phase II and Phase III).

There are several facts of clinical importance that have not been detailed under the headings of the three phases. These will be mentioned briefly.

First, do not assume that because a diet is correct for a patient in the month of May, that it will be satisfactory in September (concomitant allergy to ragweed). Continuing, do not predicate what the diet must be in wintertime, if the diagnosis has been made and the patient freed of all symptoms in the summer months.

Second, patients with primary food allergies must follow their diets any place in the country to remain symptom-free, while those with concomitant reactions may use foods with impunity in certain areas.

Third, the degree of a patient's inherent tolerance to foods can be judged best by the response upon testing the ten most common foods in the diet. If over 50 per cent of these cause trouble, as the percentage increases, the inherent tolerance is lower, while if over 50 per cent are compatible as the percentage agreeable increases, the inherent tolerance is higher. A patient with a low inherent tolerance for foods is a difficult patient to handle. He must not be restricted as much in his diet as the patient with a high inherent tolerance.

There are several other features concerning food reactions that aid one in diagnosis. Severe reactions practically always start soon after ingestion. Patients who react within one hour after ingestion will have the highest percentage of symptoms commencing within five minutes after eating, the next highest at ten minutes and very few begin as late as forty-five minutes. Such reactions, even if the food is used but once, will be clinically evident for about forty-eight to as much as seventy-two hours. Again it is important to know that in over 20,000 deliberate feeding tests, no symptoms have ever been produced by the single use of a food that persisted over five days and, this only, when the patient developed either the lung or sinus secondary reaction with the production of purulent discharges.

The longer the patient has avoided the food, the less immediate and the less definite the symptoms. It becomes increasingly important to know about late reactions, i.e., the middle of the night and the next morning upon arising.

The patient cannot eat so little of a food that it is not to be considered etiologic. The keystone of allergic studies for foods is to have a patient upon a known diet, the patient being symptom-free for at least a week on such a diet. This will require a diet record. No food studies can be exploited to their fullest extent without such records.

Local reactions of the foreign protein type, whether due to vaccines, endocrine products or vitamins, exert a non-specific depression of allergic reactions for varying periods of time. Improvement following their use is not of itself an indication that the effect is specific.

Patients with inhalant allergies may have toxic symptoms from foods at a lower level of sensitization than those required to produce perennial nasal allergy or asthma. The importance of this fact is that many people have toxic symptoms from foods but do not exhibit classical allergic syndromes.

No treatment for a food allergy is adequate if the patient is told only

that he is allergic to a given food. He must be taught how, when, and where he will contact this food. Special instruction sheets are needed for corn, cottonseed, wheat, egg, milk, soybean, flaxseed and karaya gum, as well as many others.

It is useless to feed patients foods to which they are allergic in an attempt to build them up. More often than not, patients on restricted diets who lose weight, do so because they are still using foods to which they are sensitive. The use of foods to which patients are allergic will add weight by means of allergic edema, but this is not a true gain of weight.

It is to be emphasized again, that one can judge the specificity of food reactions, not by the improvement that follows their elimination, but by the effects produced by the correct testing of the food. Examples of this are common but only one need be mentioned. A patient who gave a large skin reaction to wheat was freed of all symptoms by the avoidance of wheat. He was actually allergic to malt which was not used during the omission of wheat.

SUMMARY

Food allergy is a problem which concerns all physicians, and a more general knowledge of its nature is vital to the practice of medicine.

Food sensitization is either fixed (constant) or cyclic (decreases and increases with the incidence of the food in the diet).

Cyclic food allergy may be either primary, concomitant or thermal in type. There are three distinct phases to the cycle of food sensitization and each of these has definite clinical implications.

In the practical application of the cyclic concept, it must be borne in mind that the three phases may, but often do not, develop in a precise, consecutive manner as they do following complete elimination of a food and its subsequent reëntry into the diet. Thus, the diagnostician should be on the alert for any of the three phases and will not necessarily expect their strict consequential development.

Patients must be evaluated as to their inherent degree of tolerance for foods. If this is high, restrictive diets are in order. If low, a diversified and rotating diet is better.

It is easy to destroy a patient's tolerance for foods. It is paramount that tolerance be retained for every food possible.

One is not allergic to foods unless such allergy can be demonstrated by a correctly performed food test and such reactions must be specific and constant.

Masked food allergies are a common source of error in diagnosis. They make it impossible to determine by history if foods are either agreeable or allergic for the individual. Studies to prove food allergy require individual tests. Such tests must be supported by diet records and by instruction sheets informing patients of the source and contacts with various foods.

SUMARIO

La alergia alimenticia es un problema sue toca a todos los médicos y se ve que es necesario obtener informaciónes más diversas para la medicina general interna.

La sensibilización alimenticia o fijada, a saber: constante o ciclical, señaladamente: se aumenta o se disminuye con la incidencia de alimento en la dieta.

La alergia alimenticia ciclical puede ser del tipo primario, concomitente o termal.

Existen tres distintas fases en el ciclo de la sensibilización alimenticia, y cada una de ellas tiene una importancia clínica definitiva.

Los enfermos deben ser evaluados según el grado o condición de sus tolerancia a los alimentos. Si ésta es alta, las dietas limitadas estan en regla. Si es baja, una dieta diversificada y alternativa o cambiante es mejor.

Es fácil destruir la tolerancia alimenticia del enfermo. Es de importancia que la tolerancia sea retenida o conservada para cada alimento, posible.

Un individuo no se llama alérgico a los alimentos al menos que tal alergia pueda ser demostrada por una prueba a los alimentos correctamente hecha, y al menos que tales reacciones sean específicas y constantes.

Las alergias alimenticias enmascaradas son las comunes causas de los yerros en la diagnosis. Ellas son responsables de la causa por no poder determinar por la historia, si los alimentos son agradables o alérgicos para el individuo.

Se necesitan pruebas individuales para demostrar la existencia de la alergia alimenticia. Tales pruebas deben ser soportadas por recuerdos dietéticos y por informaciones por escrito, informando a los enfermos del origen y de los contactos con diversos alimentos.

BIBLIOGRAPHY

1. Vaughan, Warren T.: Practice of Allergy. Page 59. St. Louis: C. V. Mosby, 1939.
2. Vaughan, Warren T. The diagnostic problem in food allergy. Am. J. M. Sci., **182**:459-467, (October) 1931.

PENICILLIN FOR THE PUBLIC

(Condensed from *Science News*, April 15, 1944)

Sufficient penicillin to treat all urgent civilian cases should be available in the near future according to Robert D. Coghill, Chief of the Fermentation Division of the U. S. Department of Agriculture.

The commercial production of penicillin has been increased over a hundredfold the past year. This has been greatly stimulated by the discovery by Dr. A. J. Moyer of the action of corn steeping liquor on the growth of the mold. The cost of 100,000 units of penicillin has been reduced from $20.00 to $3.25 and will undoubtedly go much lower. There are now twenty-one of these penicillin-producing fermentation plants being erected in this country and Canada. It is estimated that when completed, these plants will produce a sufficient amount of penicillin to treat approximately 250,000 serious cases per month. This will be the means of saving thousands of lives, to say nothing of arms and legs of our fighting men.

SENSITIVITY TO MINOR POLLENS

HARRY L. ROGERS, M.D., F.A.C.A.
Philadelphia, Pennsylvania

IN eastern Pennsylvania, any pollen other than ragweed or grass is a minor pollen. Relatively few persons are sensitive to them. Botanically, they differ from the major pollens because the season is shorter, the atmospheric concentration is much less, and is much more variable from year to year.

In early spring, the minor pollens come from trees. There is usually a week of high atmospheric concentration, but this is likely to vary greatly with the distance from a forest. In three years of differential atmospheric pollen counts, we have at no time seen any prolonged concentration such as is the rule with grass and ragweed. There are occasional peaks during which the count for one day may be much greater than is usually seen in ragweed and grass. The tree and grass seasons usually overlap.

During the grass season plantain and sheep sorrel appear. In spite of the fact that the plants continue to bloom throughout most of the summer, the pollen is found on the atmospheric slides for only about three weeks. The concentration on any particular day is never more than about 25 per cent of the grass and the total count for the season is also about 25 per cent of the grass. During the ragweed season Chenopod pollen appears but in concentration of only about 10 per cent of that of ragweed. Hops appears in somewhat greater concentration and deserves further study. Cocklebur and Artemesia are close relatives of ragweed, and the Prausnitz-Kustner bodies of the former are interchangeable with those of ragweed. It is probable that hyposensitization with ragweed will also give protection against its relatives.

Plantain has been a recognized cause of hayfever for many years. It was among the first of the minor pollens to be recognized and has been used as a routine skin test on all persons suffering from early summer hay fever. For these reasons it was chosen for a detailed study. It is thought that the facts obtained from this study will apply to all the minor pollens.

We have found 102 persons with positive skin reactions to plantain in private practice. These persons may be divided into six groups:

Group 1.—Those in whom the plantain is the primary and sole cause of hay fever. These persons had a history of about four weeks of hay fever, chiefly in the month of June. They all had strongly positive skin and eye reactions to plantain and entirely negative reactions to grass and tree pollens. They all responded to specific pollen treatment.

Only two of the present series come under this group, although two entirely similar cases were seen at the Jefferson clinic.

Group 2.—Another small group (five) whose season corresponded to the first group but who had a positive but very much weaker reaction to grass or tree pollen. In this group plantain may be regarded as the major

synergen and grass as the minor synergen. Unfortunately all but one of these persons were treated with a mixture of grass and plantain.

Group 3.—A much larger series in whom the grass reaction was equal to, or more often greater than, the plantain reaction. This group was composed of fifty-four persons. Eight were treated with grass alone for one or more seasons and then were treated with a mixture of grass and plantain. Six of these obtained a better result when the mixture was used than in the previous years when grass alone was used.

Group 4.—A group of sixteen in whom the plantain reaction was only one of a large number of positive skin reactions to pollens (chiefly the trees) appearing in the spring and early summer. In almost all, sorrel and grass were also positive.

Hay fever caused by pollen from a simple species of tree occurs but is as rare as that due to plantain alone. It responds very easily to specific treatment. It is much more common to find a positive reaction to four, five or more trees as well as reactions to plantain, sheep sorrel and grass pollen.

This group has been particularly difficult to treat. The worst period is the first two weeks in May. Our treatment has consisted in injections of two mixtures, the first containing those trees to which the person gives the strongest skin reactions and the second a mixture of grass and plantain and sorrel. In spite of these painstaking and elaborate preparations, the results are too often disappointing.

Group 5.—A small group of sixteen typical late hay fever (ragweed) sufferers who have what appears to be a relatively unimportant skin reaction to plantain. This group is not nearly so large as those with similar unimportant reaction to grass.

Most of these persons do not have any symptoms in the spring. A few have mild nasal irritation and were treated with a few phylactic doses of plantain. None had enough trouble to justify the usual prophylactic treatment.

Group 6.—Another small group of nine who came to us with serious allergic symptoms throughout the year. Three had no history of hay fever. Six had very mild hay fever, not sufficiently severe to justify treatment. We did give plantain injections to a few with apparently beneficial effect on the more serious symptoms. One of this group died in an acute asthmatic seizure.

The possibility of a cure after specific treatment is much greater in plantain sensitivity than it is in either grass or ragweed. Furthermore, diminution or disappearance of the skin reaction is the rule rather than the exception. In the present series, forty-three had a reasonably complete prophylactic course of plantain injections. In twenty-three the skin reaction was distinctly reduced the following spring and in two, it was rated as negative.

In one instance the skin reaction to plantain entirely disappeared after

six years of specific treatment only to reappear and become clinically active after seven years. This was a woman forty-seven years of age who suffered from both early and late hay fever for twenty-five years. She was treated with both grass and plantain from 1929 to 1931, inclusive with an excellent result. In 1932 the skin reaction to plantain disappeared and she was treated with grass only from 1932 to 1936, inclusive. The result was excellent from 1932 to 1935 but only mediocre in 1936. The skin reaction to plantain became positive again in 1935. This year, however, she received grass treatment alone with only a fair result. In 1937 plantain was again added to the treatment and the former excellent result obtained.

Of the 102 who reacted to plantain, fifty-five also reacted positively to sheep sorrel. We have seen but one person who reacted to sorrel and not to either plantain or grass. This was a very weak reaction and was probably the cause of a very mild hay fever.

Another person had a much stronger reaction to sorrel than to grass. However, she had been receiving perennial treatment elsewhere with grass pollen with only mediocre results. She probably corresponds to our second group and the sorrel had acted as the major synergen. We believe that sorrel frequently acts as a minor synergen, particularly in those with the tree, grass or plantain reactions. When positive it should be added to the grass and plantain mixture.

Likewise, a simple tree as the sole cause of hay fever is rare but does occur. In our district, oak is most common, sycamore is next.

We had one woman with an unusually strong reaction to willow and only weak reactions to other pollens. Treatment was unusually successful and before her death from cancer, the skin reaction to willow had become completely negative.

Fifty-six reacted to ragweed. In twenty-two the reaction was of little importance, hay fever being absent or nearly so during August and September. Thirty-two, in addition to actual hay fever in the early summer, had sufficiently severe symptoms in the fall to justify treatment. It is interesting to note that all those in the fourth group (sixteen persons), with multiple tree reactions, had annoying symptoms from ragweed. In the fifth group (also sixteen persons) ragweed hay fever was the reason for consulting us and the reactions to spring pollens were unimportant.

Of the inhalants encountered throughout the year, there were eighty-one positive reactions to house dust, twenty-nine to orris root, seventeen to feathers, and eleven to animals. Thirty-one had minor nasal symptoms throughout the year, but only thirty-four had distressing symptoms.

Whenever a reaction to one of these year around substances was found, treatment was started immediately. This consisted in avoidance of the substance during the season and usually hyposensitization. House-dust extract was used in treatment in fifty-five and orris root in thirteen. We believe it is well worth the additional effort.

CONCLUSIONS

In eastern Pennsylvania—

1. Pollens other than grass and ragweed are rarely the sole cause of hay fever.

2. They frequently complicate or act as minor synergens to the major pollens.

3. Treatment is more satisfactory than it is for the major pollens.

4. "Cures" and diminution in the intensity of the skin reaction are more common than in the major pollens.

CONCLUSIONES

1. Otros pólenes, fuera de los de las Gramíneas y Malezas (Ambrósias), son raramente los únicos responsables de la fiebre de heno o polinosis.

2. Ellos frecuentemente hacen complicar o se conducen como sinérgenos menores a los pólenes principales o mayores.

3. El resultado del tratamiento es mucho más satisfactorio que en los pólenes principales.

4. En estos pólenes se encuentra, ordinariamente, más "curas" y diminución en la intensidad de la reacción cutánea, que en los pólenes principales.

A LETTER FROM THE FRONT*

Dr. Alexander Altose wrote from the New York Port of Embarkation, January 22, 1944. . . . "You might be interested in my story and wanderings. Since last June, when I left California, I have traveled over 30,000 miles in every sort of conveyance from jeep to ship to transport plane. I spent a few weeks at the Station Hospital at Camp Kilmer, New Jersey, and there helped a bit in the Allergy Clinic. Since then, I have been to North Africa and to the British Isles. I have seen several countries, the best of which is, naturally, the good old U. S. A.

"I shall leave again in a few days for another voyage. My duties are those of a transport surgeon—a good job but a far cry from allergy. I do miss the allergy, as there is plenty of it to be done in the Army, but I do as I am told. There is a big job to be done overseas and fellows like myself must expedite it. Meanwhile, you allergists at home will keep the field active and thus help give us something to which to return.

"I hope to resume contact with my books and journals this Spring and am anxious to read the back issues of THE ANNALS."

*Letters are welcome from those in the service. Please send more of them.

PRELIMINARY PROGRAM

First Annual Meeting

American College of Allergists

June 10 and 11, 1944
Palmer House
Chicago, Illinois

95th Annual Meeting, American Medical Association, Palmer House, Chicago, June 12-16, 1944

10th Annual Meeting, American College of Chest Physicians, Stevens Hotel, Chicago, June 10-12, 1944

NOTE: The papers will not necessarily be presented in the order indicated in this preliminary program and the titles of the papers and authors are also subject to change.

—*Photograph by Fabian Bachrach*

Sanford Burton Hooker, M.D.

Boston, Massachusetts

Guest Speaker, 1944

Preliminary Program

Saturday, June 10, 1944

Breakfast

(Place to be announced)—7:30 to 8:30 a.m.

Members of Board of Regents and Program Committee

Registration

Fourth Floor—8:00 a.m.

Instructional Courses

Club Floor—8:30 to 10:30 a.m.

Otorhinolaryngologic Allergy—FRENCH K. HANSEL, M.D., St. Louis, Missouri (Room 14)

Pediatric Allergy—JEROME GLASER, M.D., Rochester, New York; CHARLES S. MILLER, M.D., Corona, New York (By invitation); MARION B. SULZBERGER, Commander (MC) USNR, New York, New York (By invitation); RALPH BOWEN, M.D., Houston, Texas (Room 18)

Gastro-Intestinal Allergy—ORVAL R. WITHERS, M.D., Kansas City, Missouri (Rooms 15 and 16)

Allergy of the Central Nervous System—T. WOOD CLARKE, M.D., Utica, New York, and J. WARRICK THOMAS, M.D., Cleveland, Ohio (Room 17)

Symposium on Service Allergy

Red Lacquer Room—10:30 a.m. to 1:00 p.m.

Allergy in the Army—COLONEL SANFORD W. FRENCH, (MC) USA, 4th Corps Command, Atlanta, Georgia, and MAJOR LAWRENCE T. HALPIN, (MC) AUS, 4th Corps Command, Atlanta, Georgia

Commentator: LT. COL. L. E. LIEDER, Army Service Forces, Walter Reed General Hospital, Washington, D. C.

Allergic Dermatoses in the U. S. Navy—COMMANDER MARION SULZBERGER, (MC) USNR, New York, N. Y. (By invitation)

Commentator: LT. MORRIS LIEDER, (MC) USNR, Dispensary, U. S. Naval Air Station, Pensacola, Florida (By invitation)

Allergic Dermatitis in War Industries—LOUIS SCHWARTZ, M.D., Medical Director, U. S. Public Health Service, Bethesda, Maryland

Commentator: SAMUEL M. PECK, M.D., Senior Surgeon, U. S. Public Health Service, Bethesda, Maryland (By invitation)

College Luncheon

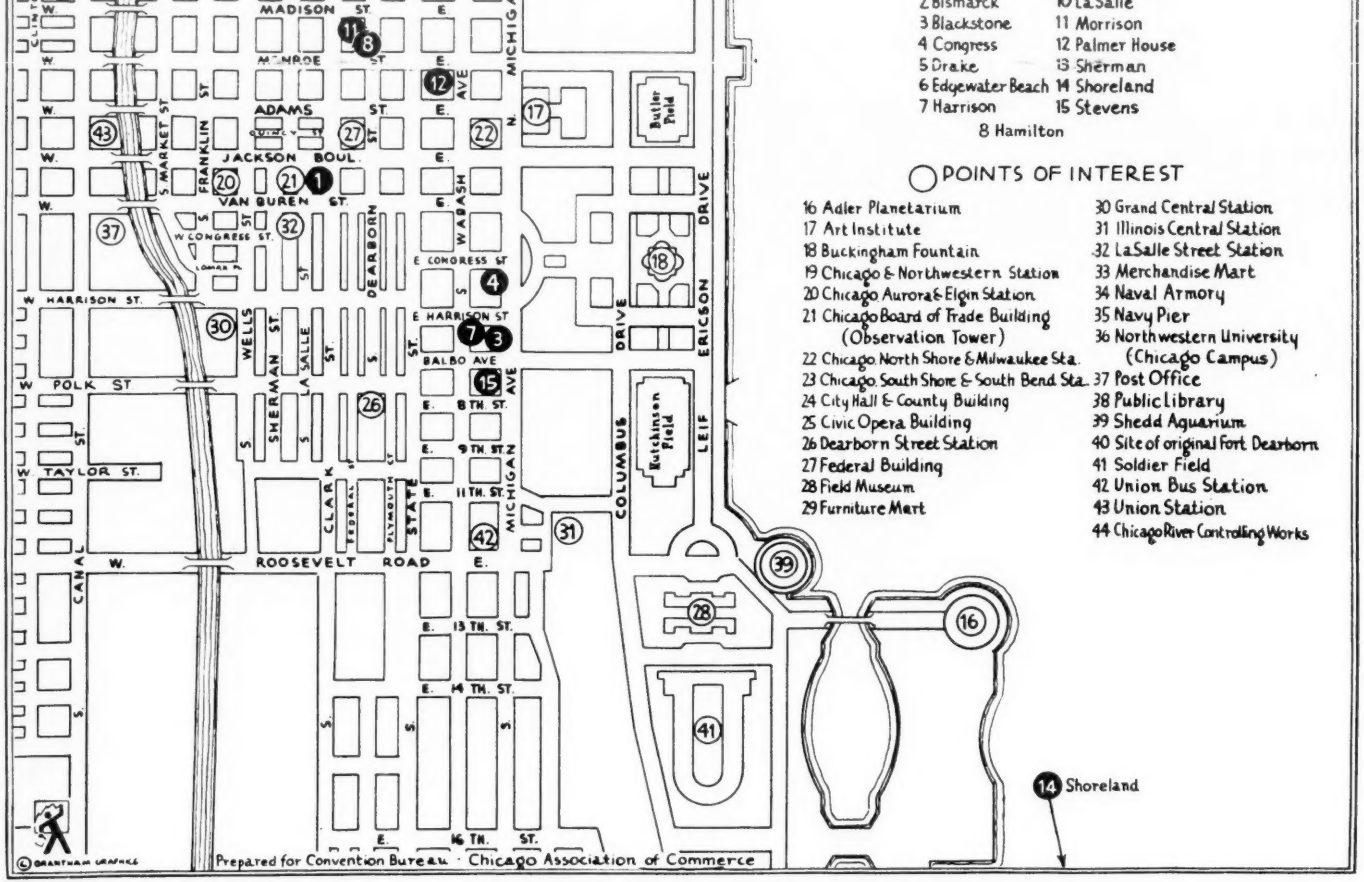
Red Lacquer Room—1:00 to 2:00 p.m.

The Physiologic, Pathologic and Immunologic Aspects of Allergy

Red Lacquer Room—2:00 to 5:00 p.m.

Address of the Guest of Honor: Qualitative Differences in Canine Dander—SANFORD B. HOOKER, M.D., Boston University, Boston, Massachusetts

Map of
DOWNTOWN
CHICAGO
Edgewater Beach
Convention and Exposition Hall
HOTELS
Members of Convention Bureau
1 Atlantic
2 Bismarck
3 Blackstone
4 Congress
5 Drake
6 Edgewater Beach
9 Knickerbocker
10 La Salle
11 Morrison
12 Palmer House
13 Sherman
14 Shoreland
E. BELLEVUE PL.
E. OAK
E. WALTON
E. DELAWARE PL.
E. CHESTNUT PL.
E. PEARSON ST.
CHICAGO AVE.
E. SUPERIOR ST.
E. HURON ST.
E. ERIE ST.
E. ONTARIO ST.
E. OHIO ST.
E. GRAND AVE.
E. ILLINOIS ST.
E. HUBBARD ST.
E. NORTH WATER ST.
KINZIE ST.
WACKER DRIVE
LAKE ST.
RANDOLPH ST.
WASHINGTON ST.
MADISON ST.
MONROE ST.
LAKE SHORE DRIVE
MICHIGAN AVE.
ORLEANS
FRANKLIN
WELLS
LA SALLE
CLARK
DEARBORN
STATE
WABASH
RUSH
CLAIR
FAIRBANKS
McCLURG CT.
N. KINGSBURY ST.
W. GRAND AVE
CLINTON ST.
N. WACKER DR.


1 Bismarck
2 Blackstone
3 Congress
4 Drake
5 Edgewater Beach
6 Harrison
7 Hamilton
8 LaSalle
9 Morrison
10 Palmer House
11 Sherman
12 Shoreland
13 Stevens
POINTS OF INTEREST
16 Adler Planetarium
17 Art Institute
18 Buckingham Fountain
19 Chicago & Northwestern Station
20 Chicago Aurora & Elgin Station
21 Chicago Board of Trade Building (Observation Tower)
22 Chicago North Shore & Milwaukee Sta.
23 Chicago South Shore & South Bend Sta.
24 City Hall & County Building
25 Civic Opera Building
26 Dearborn Street Station
27 Federal Building
28 Field Museum
29 Furniture Mart
30 Grand Central Station
31 Illinois Central Station
32 LaSalle Street Station
33 Merchandise Mart
34 Naval Armory
35 Navy Pier
36 Northwestern University (Chicago Campus)
37 Post Office
38 Public Library
39 Shedd Aquarium
40 Site of original Fort Dearborn
41 Soldier Field
42 Union Bus Station
43 Union Station
44 Chicago River Controlling Works
MADISON ST.
MONROE ST.
ADAMS ST.
JACKSON BOUL.
VAN BUREN ST.
W. CONGRESS ST.
E. CONGRESS ST
W HARRISON ST.
E HARRISON ST
BALBO AVE
POLK ST
TAYLOR ST.
ROOSEVELT ROAD
8TH. ST.
9TH. ST.
11TH. ST.
13TH. ST.
14TH. ST.
16TH. ST.
WELLS ST.
FRANKLIN ST.
MARKET ST.
DEARBORN ST.
WABASH AVE
MICHIGAN AVE
SHERMAN ST.
LA SALLE ST.
CLARK ST.
STATE ST.
CANAL ST.
COLUMBUS DRIVE
ERICSON DRIVE
LEIF
Butler Field
Kutchinson Field
14 Shoreland
Prepared for Convention Bureau · Chicago Association of Commerce

Dermatologic Manifestations of Familial Nonreaginic Food Allergy—ARTHUR F. COCA, M.D., Pearl River, New York

Physiologic Aspects of Allergy—CHARLES F. CODE, M.D., Mayo Clinic, Rochester, Minnesota (By invitation)

The Mechanism of Desensitization—J. BRONFENBRENNER, Ph.D., Washington University, St. Louis, Missouri (By invitation)

Immunologic Studies of Hay Fever—MARY H. LOVELESS, M.D., New York, New York (By invitation)

The Aerobiologic Phase of Allergy—E. C. STAKMAN, Ph.D., Chief of Division of Plant Pathology and Botany, Department of Agriculture, University of Minnesota, Saint Paul, Minnesota

Almay Cocktail Hour

Place to be announced—7:00 to 8:00 p.m.

Presented through the courtesy of Almay, Inc., New York, N. Y.

Informal Dinner

Red Lacquer Room—8:00 p.m.

Address of the President—FRENCH K. HANSEL, M.D., St. Louis, Missouri
Symphony of the Seasons (Motion picture with color and sound—symphony music) —HERBERT J. RINKEL, M.D., Kansas City, Missouri

Sunday, June 11, 1944

Breakfast

(Place to be announced)—7:30 to 8:30 a.m.

Members of Board of Regents and Program Committee

Registration

Fourth Floor—8:00 a.m.

Instructional Courses

Club Floor—8:30 to 10:30 a.m.

Dermatologic Allergy—LOUIS A. BRUNSTING, M.D., Rochester, Minnesota (Room 18)

Asthma—LEON UNGER, M.D., Chicago, Illinois (Room 14)

Drug Allergies—ETHAN ALLAN BROWN, M.D., Boston, Massachusetts (Rooms 15 and 16)

Scientific Progress in Allergy

Red Lacquer Room—10:30 a.m. to 1:00 p.m.

Chronic Urticaria in Female Castrates—CARL J. DEISSLER, M.D., San Francisco, California

Observations on Several Hundred Cases of Asthma Observed in the Station Hospital, Allergy Clinic, Fort Bliss—BERTHOLD N. STERN, *Captain* (MC), AUS, Ft. Bliss, Texas

A Method for the More Accurate Estimation of the Importance of Individual Plant Species Concerned in Pollinosis—GEORGE F. HARSH, Lt. Comdr. (MC) USNR, San Diego, California, MRS. HELEN MCMICHAEL, R.N., and MRS. JULIA KLEIN, R.N., San Diego, California

Problems in the Diagnosis of Asthma—GEORGE L. WALDBOTT, M.D., Detroit, Michigan

Chemical Evaluation of Soybean Milk and Oil in Allergic Infants and Children—ALBERT V. STOESSER, M.D., University of Minnesota Medical School, Minneapolis, Minnesota

The Allergy Problem of the Inductee, the Soldier and the Veteran—HENRY I. SHAHON, Captain (MC) AUS, Veterans Administration Facility, First Service Command Unit, West Roxbury, Massachusetts

Unusual Complications of Bronchial Asthma: Air in Extrapulmonary Areas—V. J. DERBES, M.D., Tulane Medical School, New Orleans, Louisiana

Growth and Development of Allergic Diseases. A Study of 100 Allergic Children from Infancy to Ten Years of Age—NORMAN W. CLEIN, M.D., Seattle, Washington

Serum Potassium Response to Epinephrine in Normal and Asthmatic Subjects—SUSAN C. DEES, M.D., Duke University, Durham, North Carolina

Pollinosis and Other Problems in the Practice of Allergy in Mexico—MARIO SALAZAR MALLÉN, M.D., Mexico City, Mexico

A New Technique for the Indirect Method of Skin Testing—ROBERT S. MCGRATH, M.D., Washington, D. C.

(Papers limited to 15 and 20 minutes)

RECESS

Committee Meetings

Place to be announced—2:00 to 3:00 p.m.

Board of Directors and Board of Regents

Place to be announced—3:00 to 4:00 p.m.

Annual Business Meeting

Red Lacquer Room—4:00 to 5:00 p.m.

Election of Officers—Committee Reports

PROPOSED SECTION OF VETERINARY ALLERGISTS

Organization Meeting

Friday, June 9, 1944

Room 17, Club Floor—2 to 5 p.m.

Introductory Remarks—I. FOREST HUDDLESON, D.V.M., Lansing, Michigan

Classification of the Phenomena of Specific Sensitivity in Lower Animals—CHARLES ROBBINS SCHROEDER, D.V.M., Pearl River, New York

Reaginic Allergy in Cattle—LESTER REDDIN, JR., D.V.M., Pearl River, New York

Allergy in the Dog—Allergic Rhinitis, Dermatitis and Urticaria (Illustrated by slides and colored film)—FRED W. WITTICH, M.D., and F. W. GEHRMAN, D.V.M., Minneapolis, Minnesota

Serum Sickness in Rabbits—MOYER S. FLEISHER, M.D., St. Louis, Missouri

Discussions will be welcomed

SCHEDULE OF COURSES

Saturday, June 10, 1944

Palmer House

8:30 to 10:30 A.M.

$2.00 per course

Course A-1 **PEDIATRIC ALLERGY**—Room 18, Club Floor

JEROME GLASER, M.D., Rochester, N. Y.; CHARLES S. MILLER, M.D., Corona, N. Y. (By invitation); MARION B. SULZBERGER, Cdr. (MC) USNR, New York, N. Y. (By invitation); RALPH BOWEN, M.D., Houston, Texas

Course A-2 **OTORHINOLARYNGOLOGIC ALLERGY**—Room 14, Club Floor

FRENCH K. HANSEL, M.D., St. Louis, Missouri

Course A-3 **GASTRO-INTESTINAL ALLERGY**—Rooms 15 and 16, Club Floor

ORVAL R. WITHERS, M.D., Kansas City, Missouri

Course A-4 **ALLERGY OF THE CENTRAL NERVOUS SYSTEM**—Room 17, Club Floor

T. WOOD CLARKE, M.D., UTICA, New York, and J. WARRICK THOMAS, M.D., Cleveland, Ohio

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Sunday, June 11, 1944

Palmer House

8:30 to 10:30 A.M.

$2.00 per course

Course B-5 **DERMATOLOGIC ALLERGY**—Room 18, Club Floor

LOUIS A. BRUNSTING, M.D., Mayo Clinic, Rochester, Minnesota

Course B-6 **ASTHMA**—Room 14, Club Floor

LEON UNGER, M.D., Chicago, Illinois

Course B-7 **DRUG ALLERGIES**—Rooms 15 and 16, Club Floor

ETHAN ALLAN BROWN, M.D., Boston, Massachusetts

THE MOLAR STANDARDIZATION OF RAGWEED POLLEN EXTRACTS

GEORGE E. ROCKWELL, M.D., F.A.C.A.

Cincinnati, Ohio

NUMEROUS methods such as Noon unit,[15] dilution of extract used,[20] total nitrogen,[10,12] so-called protein nitrogen unit,[11,13,14] (phosphotungstic acid precipitate nitrogen), and serological reactions,[3,4,5,8,9,21] have been used for standardizing pollen extracts. However, none of these methods are entirely satisfactory as it has been practically impossible to prepare different extracts of pollen which are clinically interchangeable.

Standardizing solutions on a chemical basis may be done in several ways, namely, as normal solutions, as molar solutions, or on their oxidizing or reducing capacities. Standardization of pollen extract by one of these chemical methods would be scientifically accurate and would make it possible to reduplicate or interchange extracts. However, ragweed pollen extract contains more than one antigen; therefore, standardization on the molar basis would involve the standardization of a solution containing a mixture of substances. Under certain conditions this is feasible and accurate providing certain information concerning the composition of the substances is known.

With this in mind let us review the chemical composition of the ragweed pollen antigen. In previous papers[16,17,18] we have shown that the major antigen in ragweed pollen extract has a molecular weight of 4496, and each molecule contains thirty-eight nitrogen atoms of which two are free a-amino nitrogen atoms. In addition to this major antigen we have shown that there are four lesser antigens with molecular weights of 1,000 or thereabouts. These low molecular weight antigens contain from two to nine nitrogen atoms per molecule of which one is a free a-amino nitrogen atom. These findings are in keeping with those reported by Abramson [1,2] who described a major antigen having a molecular weight of approximately 5,000 and several pigmented minor antigens having much lower molecular weights.

In Table I are listed the more important chemical data concerning the antigens found in crude ragweed pollen extract. From this table we note that the molecular weight of the major antigen, Fraction 1, is over four times greater than the average molecular weight of the four minor fractions. From the column in Table I designated "No. of Nitrogen Atoms per Molecule," it is readily seen that there is an appreciable difference between the various fractions; Fraction 1 containing approximately 65 per cent of the total nitrogen with the remaining 35 per cent being distributed among the lesser antigens. From the column "No. of Free a-Amino Groups per Molecule" the unique distribution is at once noted, namely that Fraction 1 contains two free a-amino groups per molecule

TABLE I. A SUMMARY OF THE CHEMICAL NATURE OF THE VARIOUS FRACTIONS OF RAGWEED POLLEN EXTRACT.

Fraction	Molecular Weight	No. Flavonol Radicals in Each Molecule	No. Amino Acids Per Molecule	No. Nitrogen Atoms Per Molecule	No. of Free A-Amino Groups Per Molecule	Per Cent of Total Nitrogen Which is Free A-Amino Nitrogen
1	4496	1	28	38	2	5.26
2	1096	1	6	6	1	16.66
3	951	1	3	3	1	33.33
4	651	1	2	2	1	50.00
5	1123	1	4	9	1	11.11

while the lesser antigens each contain only one free a-amino group per molecule.

Thus, we find two main groups of antigens in ragweed pollen extract: Group A (Fraction 1) which has a high molecular weight and contains a large number of nitrogen atoms per molecule of which two are free a-amino groups; and Group B (minor antigens) which has an average molecular weight of approximately 1,000 and contains a small number of nitrogen atoms of which only one is a free a-amino group per molecule. Because the big immunological differences are between Groups A and B rather than between the members of Group B, it is feasible and practical for our present purposes to consider these antigens in the two groups. Table II shows the data of Table I rearranged on this basis. From Table II it can readily be seen that by determining the total amount of nitrogen and the total free a-amino nitrogen *in the active antigen* in the pollen extract any of the data in Tables I or II can be computed.

The phosphotungstic acid precipitate is a convenient and practical method of separating the active antigen from the crude extract. Cooke recognized this when he proposed the so-called protein nitrogen unit. However, Brown and Benotti[7] state that the removal of the phosphotungstic acid precipitate does not entirely remove the skin-test-reactive material from the supernatant fluid. In concentrated extracts after the complete removal of the phosphotungstic acid precipitate (with the aid of thorough chilling after the reaction has been completed), we have found that if the remaining phosphotungstic acid is removed from the supernatant fluid by repeated extraction with ether and the excess acid neutralized, then the supernatant fluid contains less than 2 per cent of its original concentration of skin-reactive material. Although the phosphotungstic acid precipitate of ragweed pollen extracts may not absolutely represent the active pollen antigen, it still is the most convenient and

TABLE II. SHOWING IMPORTANT COMPONENTS OF THE TWO GROUPS OF ANTIGENS IN RAGWEED POLLEN EXTRACT.

Group	Molecular Weight	Total Nitrogen Atoms Per Molecule	No. of Free A-Amino Nitrogen Atoms per Molecule	Per Cent of Total Nitrogen Which is Free A-Amino Nitrogen
A (Frac. 1)	4496	38	2 (A)	5.26
B average	955	5	1	20.00
1 Mol. A & 4 Mols. B		58 (T)	6 (X)	10.345

practical method available. Therefore, we have used this method in the following experiments for obtaining the total and the free a-amino nitrogen of the active antigen.

Calculation of Distribution of the Free A-Amino Nitrogen—
Where

T=total nitrogen of both A and B (PTA ppt. nit.)
X=total free a-amino nitrogen of both A and B (free a-amino nit. of PTA ppt.)
A=amount of free a-amino nitrogen in Group A (Fraction 1)
B=amount of free a-amino nitrogen in Group B

then

$$A=0.3568T\ (0.2-\frac{X}{T})$$

and

$$B=X-A$$

From the above equations we are able to determine the amount of free a-amino nitrogen in the extract which represents Group A (Fraction 1) and Group B. If desired on a similar basis and without additional determinations, Fractions 2, 3, 4, and 5 can be calculated. However, for purposes of standardization in molar solution the important consideration is how much of the extract is major antigen and how much is minor antigen.

Calculation of Molar Concentration.—Group A (Fraction 1): Knowing the amount of free a-amino nitrogen in the extract which is due to Fraction 1 we can calculate its molar concentration since we know that each molecule contains 2 free a-amino nitrogens. Thus, a one molar solution would contain 28.016 grams of free a-amino nitrogen per liter or 28.016 mgs. per ml.

Hence where

A=amount of free a-amino nitrogen in Group A

then

$$AM \text{ (Fraction 1 Molar Concentration)} = \frac{A}{28.016}$$

and for Group B, since it contains only 1 free a-amino group per molecule

$$BM \text{ (Group B Molar Concentration)} = \frac{B}{14.008}$$

$$TM \text{ (Total Molar Concentration} = AM + BM$$

Calculation for Converting to Molar Units.—But such molar expression would be confusing to the allergist who is used to units or dilutions, therefore, we have converted the above to molar units.

For convenience a new unit chosen should approximate a unit now used for standardization, hence we have selected a Molar Unit which is almost equivalent to a Noon Unit, namely 1 ml of a 4×10^{-8} molar solution; thus:

$$AMU \text{ (Fraction 1 Molar Units)} = \frac{AM}{4 \times 10^{-8}}$$

$$BMU \text{ (Group B Molar Units)} = \frac{BM}{4 \times 10^{-8}}$$

$$TMU \text{ (Total Molar Units)} = AMU + BMU$$

Combining these equations with those given under "Calculation of molar concentration" we have:

AMU=892,000.A
BMU=1,785,000.B
TMU=AMU+BMU

Résumé of Determinations and Calculations Necessary for Molar Standardization.†—Thus in the molar standardization of ragweed pollen extract it is only necessary to make two determinations:

(1) Total nitrogen in PTA ppt.=T
(2) Free a-amino nitrogen in PTA ppt.=X

and use the following equations:

(1) $A = 0.3568T \left(0.2 - \frac{X}{T}\right)$

$B = X - A$

(2) AMU=892,000.A
BMU=1,785,000.B
TMU=AMU+BMU

EXPERIMENTAL

Method.—The phosphotungstic acid precipitate was prepared by taking an aliquot amount of the extract (3 to 10 ml. depending upon the concentration of the extract) to which was added sufficient concentrated HCl to give a final concentration of 10 per cent and sufficient phosphotungstic acid solution to give a final concentration of 5 per cent. This

†If a purified extract which contains only the active antigen (such as prepared by Efron's, Rockwell's, or other methods) is used then T, the total nitrogen, and X, the free a-amino nitrogen, should be determined directly on the purified extract and not on the phosphotungstic acid precipitate.

mixture was allowed to stand at room temperature until the reaction was complete and then placed in the ice box at 0° C. until thoroughly chilled (for best results this requires forty-eight hours). The precipitate was separated by centrifuging, and then carefully washed twice with 4 ml. portions of cold, ammonia-free water (preferably containing the same amount of HCl and phosphotungstic acid as the original mixture). This is essentially the method described by Block[6] for precipitation of basic amino acids.

The total nitrogen was determined by the micro Kjeldahl method and the free a-amino nitrogen by the Van Slyke Manometric method.

Analysis of Extract 1.—(Extract of an equal mixture of large and small ragweed pollen.) This analysis is given with details of calculations in order to illustrate standardization as molar units.

T (total nitrogen in PTA ppt.) = 0.4188 mg. per ml.
X (free a-amino nitrogen in PTA ppt.) = 0.05875 mg. per ml.

then since

$$A = 0.3568T\ (0.2 - \frac{X}{T})$$

$$A = 0.3568 \times 0.4188\ (0.2 - \frac{0.05875}{0.4188})$$

$$A = 0.00887$$

$$B = X - A = 0.05875 - 0.00887 = 0.0499$$

then

AMU = 892,000 × 0.00887 = 7,912
BMU = 1,785,000 × 0.0499 = 89,071
TMU = 7,912 + 89,071 = 96,983
Total nitrogen in Fraction 1 = 0.1686 mg. per ml.
or 40.23 per cent of total nitrogen in PTA ppt.
Total nitrogen in Group B = 0.2495 mg. per ml.
or 59.77 per cent of total nitrogen in PTA ppt.

Extracts of pollen differ not only with the sample of pollen but with its age, type of extracting fluid used, concentration of the extraction, reaction of the extracting fluid, and probably many other factors. This variation is not only in the actual amount of antigen extracted but also an even larger variation in the distribution of the antigens between Fraction 1 (large molecule) and Group B (small molecule). To illustrate this the analysis of another equal mixture of ragweed pollen extract is given below.

Analysis of Extract 2—

T (total nitrogen in PTA ppt.) = 0.460 mg. per ml.
X (free a-amino nitrogen in PTA ppt.) = 0.0465 mg. per ml.

therefore

A = 0.0163
B = 0.0302
AMU = 14,539
BMU = 53,907
TMU = 68,446
Total nitrogen in Fraction 1 = 0.309 mg. per ml.
or 67.17 per cent of the total nitrogen in the PTA ppt.
Total nitrogen in Group B = 0.151 mg. per ml.
or 32.83 per cent of the total nitrogen in the PTA ppt.

In comparing the two extracts it will be noted that the total nitrogen is a little higher in Extract 2 and hence the so-called protein nitrogen units would be higher. On the converse, Extract 2 contains almost 50 per cent fewer total molar units (TMU) than Extract 1, but 100 per cent more Fraction 1 molar units (AMU) than Extract 1. In Extract 2, Fraction 1 contains 67.17 per cent of the total nitrogen whereas in Extract 1 it is only 40.23 per cent. This is shown in Figure 1.

These differences clearly depict the reasons why standardization by present methods is not satisfactory; also they clearly illustrate the value and importance of molar standardization in which the number of large molecules and the number of small molecules are considered. To further demonstrate this the pollen from a previous experiment was reëxtracted. According to Roth and Nelson[19] this second extraction should contain fewer large molecules in proportion to the number of small molecules than the first extract. If standardization in molar units is accurate then standardization of this extract (Extract 3 made by re-extracting the pollen from a previous experiment) should show a marked decrease in Fraction 1 molar units (AMU) as compared to Group B molar units (BMU).

Analysis of Extract 3.—(Extract obtained from the reëxtraction of pollen previously used)

T (total nitrogen in PTA ppt.) = 0.1200 mg. per ml.
X (free a-amino nitrogen in PTA ppt.) = 0.0202 mg. per ml.

therefore

A = 0.00136
B = 0.01884
AMU = 1,213
BMU = 33,629
TMU = 34,842
Total nitrogen in Fraction 1 = 0.0258 mg. per ml.
or 21.50 per cent of the total nitrogen in the PTA ppt.
Total nitrogen in Group B = 0.0942 mg. per ml.
or 78.50 per cent of the total nitrogen in the PTA ppt.

From the analysis of Extract 3 it is quite evident that the second extraction of pollen contains much less Fraction 1 molar units (large molar units) than does the first extract and in proportion contains a much larger amount of small molar units. This not only verifies Roth and Nelson's previous observations but also checks the accuracy of standardization in molar units.

DISCUSSION

Molar standardization of pollen extract is simple and scientifically accurate; it should prove practical and useful in clinical application. It is important that pollen extracts be standardized as soon as possible after their preparation as the free a-amino nitrogen changes with the aging of the extract although there may be no change in the total nitrogen or the phosphotungstic acid precipitate nitrogen. In fact, the aging of an extract can be followed by a study of its free a-amino nitrogen.

The real value of molar standardization can only be shown by extensive clinical use of it; for this reason it is hoped that many clinicians will try this method. The writer will be glad to coöperate with any allergists wishing to use this method of standardization.

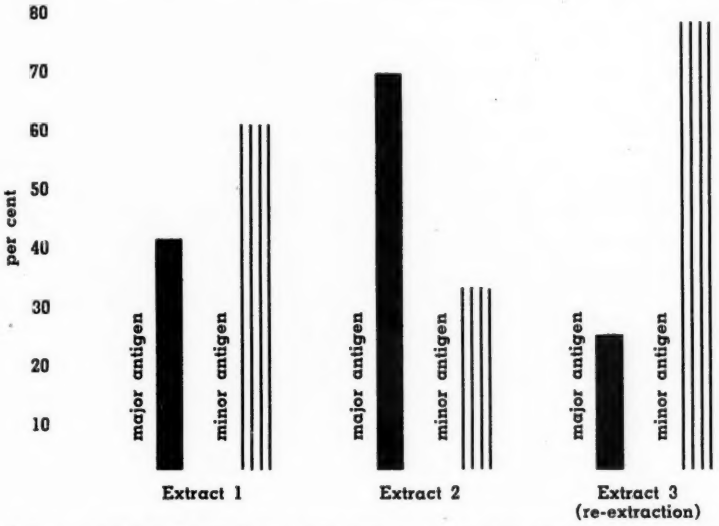

Fig. 1. Showing the percentage of total nitrogen in the phosphotungstic acid precipitate which is Major Antigen (Fraction 1) and Minor Antigen (Group B) in the various extracts.

SUMMARY

1. A method is described for the standardization of pollen extracts as molar solutions.

2. To make these molar standardizations more practical for clinical use a formula is given for the conversion of molar concentration to molar units.

3. For standardization as molar units only two determinations are necessary, total nitrogen and total free a-amino nitrogen in the phosphotungstic acid precipitate.

4. Sample analyses are given which not only illustrate exactly the standardization of pollen extract as molar units, but which also show graphically why standardization on the so-called protein nitrogen units, total nitrogen, dilutions used, or Noon Units, is unsatisfactory; and how standardization as molar units obviates these objections.

5. By studying the free a-amino nitrogen it is possible to follow the aging of pollen extracts.

6. By molar standardization it is possible to detect differences in extracts which heretofore were not apparent.

The author expresses his appreciation to Phyllis Mugavin Rohrer, whose untiring devotion to the duties of the day made this work possible.

SUMARIO

1. Se describe un método para la standardización de extractos de polen como soluciones molares.

2. Para hacer esta standardización molar mas práctica, para uso clínico se dá una fórmula para la conversión de concentración molar a unidades molares.

3. Para standardización como unidades molares, son necessarias dos determinaciones unicamente, nitrógeno total y nitrógeno a-amino libre total en el ácido fosfotungstico precipitado.

4. Se dan pruebas de análisis las cuales no solamente ilustran exactamente la standardización de extracto de polen como unidades molares, sino que tambien muestran graficamente porque standardización en el llamado unidades nitrógeno proteina, nitrógeno total, diluciones usadas o Unidades Noon, no es satisfactorio, y como standardización como unidades molares salva estas objeciones.

5. Por medio del estudio del nitrógeno a-amino es posible seguir el tiempo de envejecimiento de extractos de polen.

6. Por medio de la standardización molar es posible hallar diferencias en extractos, las cuales antes no eran aparentes.

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(Continued on Page 149)

STERILE ABSCESS COMPLICATING ALUM-PRECIPITATED TETANUS TOXOID

A Case Report

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ALTHOUGH it is generally believed that sterile abscess is a not-too rare reaction to alum-precipitated tetanus toxoid, a search of the literature by the author revealed a report on this subject by but a single group of authors.[4]

Literature on the reactions produced by tetanus toxoid is distinctly meager as compared with the number of reports on the subject of reactions to diphtheria toxoid. A discussion of the latter will therefore be included in this paper for the purpose of filling in gaps in our experience with the former.

Reactions to toxoid (diphtheria or tetanus) consist of two major types, general and local. It is not the purpose of this paper to discuss the general reaction, but in brief it consists of fever, chills, dizziness, headache, vomiting, diarrhea, muscular aches, and occasionally is accompanied by urticaria or anaphylaxis. It is generally believed that the general reaction is caused by the protein fraction of the toxoid, particularly by the Witte peptone in which the organism is grown.[15] This is particularly true of the definitely anaphylactic type of response. There is, indeed, evidence that the vast majority of reactions, both general and local, are due to previous sensitization to some part of the protein fraction of the toxoid. In a series of 949 cases receiving their first injection, Landes,[9] using fluid toxoid, reported no reactions. In a second series of mixed cases, he reported twelve reactions. Ten of these reacting patients had been previously injected. Similarly, Fulton[3] reports that local reactions are much more common in the Schick-negative than in the Schick-positive group, the former giving 86 per cent of reactions, the latter giving 42 per cent.

The local reaction consists of redness, induration, edema, pain, tenderness, and heat at and about the injection site. It may be accompanied by local lymphadenitis and occasionally by lymphangitis. The local reaction usually subsides completely in a few days, leaving no trace. Occasionally, however, the process goes on to suppuration with the formation of a sterile abscess. It is with this latter complication that this paper is principally concerned.

Sterile abscess occurs far more commonly with diphtheria toxoid than with tetanus toxoid. All cases reported have been found where alum-precipitated toxoid was used. The author has been unable to find any reports of sterile abscess following the use of formolized toxoid. Local reactions, as a whole, are far more severe following the alum-precipitated toxoid than they are following the formolized preparation.[11] A review of the literature reveals a report of two cases of sterile abscess in a series of 500 cases immunized with alum-precipitated tetanus toxoid by Gallagher et al.[4] No other paper reviewed by the author mentions this compli-

cation.[2,5,7,8,12,13] Numerous authors working with alum-precipitated diphtheria toxoid have encountered sterile abscesses, however. Harrison,[6] McGinnes,[10] and Fulton,[3] each report personal experience with this type of reaction, and the latter two quote instances of numerous cases of sterile abscess following the use of certain batches of toxoid. Personal communications[1,14] confirm the fact that a great number of sterile abscesses were encountered when alum-precipitated toxoid was first developed, and an excessive amount of alum was present in the product. Since the alum content was limited to 2 per cent, however, sterile abscesses have become rare. Sterile abscess, formerly produced in large number by improperly prepared toxoid, has now become a sign of individual idiosyncrasy.

It is known that superficial injection of alum-precipitated toxoid may frequently cause abscess formation. In fact, it is said that an abscess will almost invariably follow intracutaneous administration.[1] In this discussion, however, deep subcutaneous administration is the only type considered.

The local reactions occurring after the use of alum-precipitated toxoid may be caused either by the protein fraction as in the similar reactions following formolized toxoid, or else by the alum itself, or lastly by the combination of both, the precipitate acting as a mechanical device to hold the irritating protein products in contact with the tissue in concentrated form.[6] As mentioned previously, excessive alum was formerly a cause of sterile abscess, but with the standardized products of today, alum is probably not the cause of the isolated reactions of this type seen at present. Further discussion of the mechanism of the production of sterile abscess will be presented in the discussion of the following case.

CASE REPORT

The patient was a forty-one-year-old white man, single, Coast Guard enlisted, who gave no past history of any allergic symptoms. The past history was negative except for childhood exanthemata. Physical examination at the time of enlistment on September 10, 1942, was completely normal except for a number of missing teeth.

On October 19, 1942, he was given his first tetanus injection. This consisted of 0.5 c.c. of the alum-precipitated toxoid given by deep subcutaneous injection. The next day he reported to the medical office complaining of malaise, feverishness and running nose. His arm was sore. Physical examination revealed signs of a nasopharyngitis. There was no mention made of the patient's temperature or the appearance of his arm at the time. Throughout the next few days he improved subjectively and his temperature was recorded as normal on two occasions. On October 28, 1942, however, his temperature was 101 and he complained of his arm being very sore. The arm was treated with hot wet dressings. The next day his temperature was still 101, and the following day 100. By November 2, 1942, his temperature was normal and he was apparently symptom free.

On November 18, 1942, the patient was vaccinated for smallpox and was given his first typhoid inoculation. His second and third typhoid inoculations were given on November 25, 1942, and December 2, 1942, respectively. There was no unusual reaction to any of these procedures.

On December 17, 1942, the patient was given his second tetanus injection, which consisted of 0.5 c.c. of alum-precipitated toxoid given by deep subcutaneous injection. On December 22, 1942, he was admitted for treatment at the medical office because of a sore arm. He stated that for two days following the injection he had had feverishness, malaise, and vomiting. Examination showed an indurated, red, pointing area measuring 2 cm. by 2 cm. on the lateral aspect of the right arm. This was treated with hot soaks. On the following day the abscess was incised and 10 c.c. of pus evacuated. A drain was inserted. Hot dressings were continued and the drain gradually removed. By January 5, 1943, the lesion was completely healed. No examination of the pus was done.

On November 9, 1943, the patient was given his "booster" tetanus injection which consisted of the same amount of alum-precipitated toxoid administered in a similar manner. On November 15, 1943, the patient returned to the medical office complaining of a painful area on his left arm at the site of the injection. He stated that he had again been feverish, and had vomiting and generalized muscular aches immediately following the injection, and persisting for two days. He was not absent from work, however. Examination revealed an area of redness, tenderness, and induration measuring 3 cm. in diameter over the left deltoid. There was a furuncle at its center, and a large tender node in the left axilla. The patient's temperature was 37.3. He was treated by bed rest, hot soaks, and sulfathiazol, 1 gram q.i.d. The induration had decreased by the next day and treatment was continued another twenty-four hours. The following day some fluctuation was evident and the patient stated that a large amount of yellow pus had escaped spontaneously. On November 18, 1943, the abscess was incised and 15 c.c. of yellow pus evacuated. The wound was packed with iodoform gauze. It continued to drain for several days and by November 28, 1943, was completely healed. A culture of the pus on plain agar showed no growth after one week.

Because of the necessity for finding some way to immunize this individual against tetanus in line with the standard Coast Guard routine, the need became apparent for finding out just which constituents of the toxoid the patient reacted to. Consequently, on December 1, 1943, 0.25 c.c. of 4 per cent alum solution in distilled water (twice the concentration allowed in commercial toxoid) was injected into the deep subcutaneous tissue of the right arm. At the same time 0.5 c.c. of formolized toxoid was injected in the left arm. The following day the patient complained of nausea, vomiting, and malaise. His temperature was 100.8. There was no reaction on the right arm, but the left arm (into which the toxoid had been injected) presented a severe reaction with a zone of tenderness, erythema and edema measuring four inches in diameter. Bed rest was prescribed. The following day the patient's temperature was 100.4. His general symptoms persisted unabated and he then had diarrhea as well. The right arm showed no reaction except minimal point tenderness whereas the left arm showed a slightly greater local reaction than previously with an enlarged tender left axillary node, and a lymphangitic streak extending up the inner side of the left arm. From this point on, the general and local symptoms subsided until by December 8, 1943, all reactions had subsided. Fluctuation was never noted.

DISCUSSION

Hitherto it was believed that alum was the chief abscess producer in the precipitated toxoid. This was undoubtedly true in former days when large numbers of sterile abscesses were seen following the use of toxoids with a high alum content. The case just described, however, indicated another mechanism in the cases seen today, which are probably cases of individual idiosyncrasy. This patient did not react at all to alum even though the administered concentration was twice the standard. On the

other hand, he was extremely sensitive to the toxoid itself, responding with definitely allergic symptoms, both local and general.

The alum-precipitated toxoid consists of a suspension of precipitated particles, whereas the formolized toxoid is a clear fluid. The difference in the type of reaction to the two preparations is easily explained on purely mechanical principles. The particles of the former hold the allergen in constant contact in considerable concentration with the same small area of tissue, whereas the fluid toxoid easily diffuses over a wide area. Hence the former produces a localized abscess, while the latter gives a diffuse reaction. In either case the offending substance is the same, namely, an allergenic protein substance.

As for the future treatment of the case just presented, it would seem that fluid toxoid would be but a poor substitute for the material used, as the offending agent would still be present and capable of producing a severe reaction, even though of a different type. The possibility of omitting active tetanus immunization in these cases is one which should be considered.

SUMMARY

1. Reactions to alum-precipitated and formolized toxoids are discussed.

2. A case of recurring sterile abscess complicating alum-precipitated tetanus toxoid is presented.

3. The distinction between the former and the present cause of sterile abscess is made.

4. The problem of prevention of sterile abscess is considered.

SUMARIO

1. Se han discutido las reacciones al alumbre-precipitado y a los toxoidos formolizados.

2. Se ha presentado un caso de un absceso estéril recurrente, complicando el alumbre-precipitado de tétanus toxóido.

3. Se ha hecho la distinción entre la anterior y presente causa del absceso estéril.

4. Se ha considerado el problema de la prevención del absceso estéril.

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Molar Standardization of Ragweed Pollen Extracts

(Continued from Page 144)

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To the fifty reported cases of sensitivity to liver extract, the authors add eleven more. Their findings are tabulated, and among other things emphasize that the commercial brand of the extract has no relation to the incidence of reactions. In most patients, the reaction occurs rarely after the very first injection, or, if it does not appear initially, comes on when there has been a long interval since the termination of a previous course of injections. There are many more mild reactions than the published reports would indicate, the most common reaction being urticaria. Skin testing is not an absolute criterion since the intradermal test with the extract is difficult to interpret; although the authors feel that a wheal with pseudopods over 15 mm. in diameter is to be taken as a positive reaction when less than 0.05 c.c. of the material is used for skin tests. The authors feel that unit dosage should be the governing factor in the prevention of future reactions in sensitive individuals; and recommend desensitization with subsequent injections. These should be given in small doses and at more frequent intervals; at least once weekly.

L. J. H.

French K. Hansel, M.D.
Saint Louis, Missouri
President, 1944

Editorial

THE ANNUAL MEETING

Elsewhere in this issue is published the preliminary program of the First Annual Meeting of the American College of Allergists, to be held at the Palmer House, Chicago, June 10 and 11, 1944. The American College of Chest Physicians will hold their Tenth Annual Meeting at the Stevens Hotel, Chicago, June 10-12, and the American Medical Association session will be held at the Palmer House, June 12-16.

The scientific exhibits of the AMA will be located on the fourth floor of the Palmer House, and the industrial exhibits at the Stevens Hotel.

Thus, in six days an unusual opportunity is afforded the medical profession to combine intensive instruction with diversion and relaxation.

Seven excellent instructional courses will be given by the College on Saturday and Sunday mornings, June 10 and 11. Saturday morning, from 8:30 to 10:30, Dr. French K. Hansel, Washington University School of Medicine, will conduct the course on Otorhinolaryngologic Allergy; Dr. Jerome Glaser, of Rochester, New York, the course on Pediatric Allergy with Dr. Charles Miller, Corona, Long Island, Commander Marion Sulzberger (MC) USNR, and Dr. Ralph Bowen, Houston, Texas, as collaborators. At the same time Dr. T. Wood Clarke, Utica, New York, and Dr. J. Warrick Thomas, Cleveland Clinic, will conduct a course on Allergy of the Central Nervous System—Doctor Clarke's lecture will be devoted to Cerebral Allergy and that of Doctor Thomas to Ocular Allergy and Allergic Headaches; Dr. Orval Withers, University of Kansas Medical School, will head a course on Gastro-Intestinal Allergy at this time. On Sunday morning, from 8:30 to 10:30, Dr. Louis A. Brunsting, Mayo Clinic, will conduct a course on Dermatologic Allergy; Dr. Leon Unger, Northwestern University Medical School, will lead a course on Asthma, and Dr. Ethan Allan Brown, New England Medical Center, Boston, one on Drug Allergy.

These courses will be practical and devoid of formal discussion, allowing the instructor to present the subject uninterrupted. The leaders are widely experienced teachers in their field so that the registrants should have their knowledge greatly refreshed and be stimulated to do more thorough work when applying allergy to their practice. It is hoped that all the members of the College, as well as candidates and nonmembers, will take advantage of this opportunity and register early. Excellent facilities have been arranged for these courses on the Club Floor of the Palmer House.

The Symposium on Service Allergy, Saturday morning, following the instructional period, will be conducted by the leaders in their respective

fields in allergy in the Military and Public Health Service. War problems in allergy will be featured. The vast amount of material at hand and the use of standard methods make these observations invaluable and unique in the history of allergy.

Colonel Sanford W. French (MC) USA, and Major Lawrence J. Halpin (MC) AUS, Fourth Corps Command, Atlanta, will present statistics covering thousands of cases from their 84 allergy stations when discussing Allergy in the Army. Lt. Col. L. E. Lieder, Army Service Forces, Walter Reed General Hospital, Washington, D. C., will be the commentator.

Commander Marion Sulzberger (MC) USNR, New York, will discuss "Allergic Dermatoses in the U. S. Navy," and will have Lt. Morris Lieder (MC) USNR, Dispensary, U. S. Naval Station, Pensacola, Florida, as commentator.

Dr. Louis Schwartz, Medical Director, U. S. Public Health Service, Bethesda, Maryland, will discuss "Allergic Dermatitis in the War Industries," with Dr. Samuel M. Peck, Senior Surgeon, U. S. Public Health Service, Bethesda, as commentator.

The College is indeed fortunate to obtain such an array of talent for its first annual convention.

Another leading feature of Saturday's program is the Scientific Section, commencing at two o'clock. The Guest of Honor, Dr. Sanford W. Hooker, Professor of Immunology, Boston University Medical School, will be introduced by the President of the College, Dr. French K. Hansel, when Doctor Hooker will open the program with a scientific address. At this session there will be five other 25-minute papers read mainly on the Physiologic, Pathologic and Immunologic Aspects of Allergy. The participants are Dr. Arthur F. Coca, Lederle Laboratories, Pearl River, New York; Dr. Mary H. Loveless, The New York Hospital, New York City; J. Bronfenbrenner, Ph.D., Professor of Bacteriology, Washington University School of Medicine, St. Louis; Dr. Chas. F. Code, Professor of Clinical Physiology, Mayo Foundation Graduate School of the University of Minnesota, Rochester; E. C. Stakman, Ph.D., Chief, Department of Plant Pathology and Botany, Department of Agriculture, University of Minnesota, Saint Paul.

Following the Scientific Session, Saturday evening will be given over to relaxation and social informalities preceded by a cocktail hour of good fellowship. There will be an informal dinner after which President Hansel will make a short address preceding the feature entertainment of the evening. Dr. Herbert Rinkel, Kansas City, will show his famous motion picture with color and sound (symphony music) "Symphony of the Seasons." This unusual classic leaves a pleasant memory with all who have been fortunate to see it.

Sunday morning, following the instructional courses, a series of ten short, practical papers will be read by members of the College, covering a wide field of allergic diseases.

Sunday afternoon will be devoted to a regular business meeting with election of officers, reports of committees, et cetera.

Last but not at all least, an attractive program for the ladies has been arranged under the chairmanship of Mrs. Leon Unger. There will be headquarters for the ladies where they may register and become acquainted, and some enjoyable features are being planned.

Since many of the College members are in the Service and very few on this honor list can be present, all those not in the Service should consider it their duty to unify and promote the specialty of allergy at home by attending this first epochal meeting of the College.

OUR GUEST SPEAKER

Dr. Sanford B. Hooker, guest speaker at the first annual meeting of the American College of Allergists, has been attracted to science since his graduation from Dartmouth College in 1909. He received his Ch.B. from Boston University in 1912, and in 1913 received the degree of Doctor of Medicine, *magna cum laude*, after four years of an impressive academic career. Boston University School of Medicine numbers him among its most distinguished alumni.

Upon graduation, Dr. Hooker started advanced studies under Theobald Smith, William H. Park, Ludwig Hektoen, and Frederick P. Gay. In 1916 he received the degree of A.M. from the University of California. Already a research-associate at the Evans Memorial Hospital in Boston, he remained in that position until in 1918, when Base Hospital 44 was mobilized; he was then occupied in various laboratories in France from July, 1918, until October, 1919.

On the boat returning from France, Dr. Hooker turned over in his mind the then novel group-properties of human blood, discovered by Dr. Landsteiner in 1900 but little utilized before the war. It seemed to him that if one injected rabbits with cells of Type II, and absorbed the immune serum with type I, an agglutinin specific for type II might be left, and so on. Before the boat landed, he had it all figured out. It remained only to inject the rabbits and make the tests. It worked out perfectly, except that in the process he discovered an apparent antigenic relationship between the A and B antigens, as we now call them, and discovered, too, another agglutinin which may have been anti-O, or perhaps anti-N, both unknown at that time.

From that time to this, papers have not ceased to issue from Dr. Hooker's laboratory. He became interested in diphtherial and scarlatinal immunization, in streptococci, and in human supersensitiveness. In the course of his work in the latter field, he was led to observe that the very small amount of horse serum, contained in the toxin-antitoxin mixtures used at that time to immunize against diphtheria, was sufficient to render a considerable proportion of the recipients sensitive to horse serum.

A reading of Landsteiner's papers and of H. G. Wells' Chemical As-

pects of Immunity extended Dr. Hooker's interest in the direction of immunochemistry, and since about 1930 he has published a considerable number of fundamental papers on this rapidly expanding and developing subject. Subjects such as the valence of antibody, the mechanism of the precipitin-reaction, the production of more than one quality of antibody by an antigen, and the requirements for antigenicity were discussed. Extending the work of Landsteiner in this field, he showed that antibodies to a drug such as strychnine could be produced, if the drug were properly coupled chemically to a protein-carrier and injected. In connection with the mechanism of serological reactions, a controversy, characteristic in its urbanity and dialectic skill, developed between Hooker and his followers and the "lattice" school of Marrick and of Heidelberger. While the main point at issue does not seem yet to have been settled, the discussion has undoubtedly been largely responsible for the contribution of much knowledge, and indirectly for drawing new workers (as for example the chemist Pauling) into the field.

Dr. Hooker was president of the Society for the Study of Asthma and Allied Conditions in 1935-36 and of the American Association of Immunologists in 1936-37. He is an editor of the *Journal of Immunology,* for several years was on the editorial board of the *Proceedings of the Society for Experimental Biology and Medicine,* and edited the section on immunology in the *Yearbook of Pathology and Immunology,* which appeared in 1940 and 1941.

Characteristics of Dr. Hooker have always been the rigor of his thinking and the keenness of his observation. It would be hard indeed to find one of his papers in which the conclusion did not follow logically from the evidence available. His observational skill is remarkable. In the course of an experiment designed as a routine check of a predicted effect (which effect generally comes off), he has been known again and again to notice some new fact which marks a totally new contribution to knowledge.

From instructor he was promoted to Assistant Professor of Immunology at Boston University School of Medicine in 1921, Associate Professor in 1924, Professor in 1932. He has been immunologist to the Massachusetts Memorial Hospital for many years, and a member of the Evans Memorial since about 1920. As a teacher at B.U.S.M. since 1913, Dr. Hooker is probably remembered (affectionately) by the few rather than the many. This is undoubtedly as he would wish it. To students whose eyes are set solely on a medical degree and a lucrative practice, Dr. Hooker's lectures may indeed at times have seemed positively maddening with their requirement of close attention to detail and rigorous thinking. But to the real student, interested in gaining an insight into a difficult subject and in acquiring the ability to make his own contribution, Dr. Hooker's lectures have been a delight, both for their conciseness and clarity. When given suitable student material, Dr. Hooker has shown to a rare degree the gift of teaching and inspiring, even though his own interests are

primarily in investigation. Men such as he comprise the most important contribution of our Universities to the scientific life of our times.

W. C. Boyd

VETERINARY ALLERGY

Preceding the regular session of the College at Chicago next June 10 and 11, there will be a joint informal meeting of the veterinarians representing the American Veterinary Medical Association and the members of the American College of Allergists at the Palmer House, Friday afternoon, June 9.

The *purpose* of the meeting is to organize a section of the College known as the Veterinary Section of Immunology and Allergy. The *plan* is to closely coördinate the investigative and clinical observations of immunology and allergy observed in the lower animals with those in humans in a united effort to further our knowledge of these subjects for the health betterment of both man and animal.

It is proposed that those members of the American Veterinary Medical Association who have contributed and are interested become Associate Fellows in the College; and that a regular section composed of this group of scientists and those in the College with allied interests meet annually.

At these sessions scientific papers embracing all phases of the subject, as well as round table and panel discussions, will be presented. The Executive Committee would be comprised of equal representation from both interested groups who would conduct the business affairs of the section. It is also proposed that a fund be established for stimulating research in immunology and allergy of animals. Funds and trained men are essential.

For the first meeting, a tentative program has been arranged with the informal sanction of the officials of both societies which is published in this issue. The program will be presented on the fourth floor of the Palmer House where the regular session is to be held. There has been an enthusiastic response to present papers at this first meeting of such a nature ever held which promises to be very largely attended. Dr. J. G. Hardenbergh, Secretary, American Veterinary Medical Association, headquarters in Chicago, endorses the plan.

Although chemist Pasteur, over sixty years ago, proved the value of teamwork in the various sciences, progress has been retarded by isolationism. Today, experimental anaphylaxis, clinical allergy and immunity to infection are considered by the majority of all investigators as basically the same, and each is the result of a similar underlying mechanism, whose manifestations of reaction are determined by secondary factors.

With the accumulating and increasing knowledge of immunology and allergy made available by the present war, a way should be made for a united effort of scientists for a peacetime program. All those interested are invited to attend. A tentative program appears on page 135 of this issue.

F.W.W.

Progress in Allergy

Under the direction of ETHAN ALLAN BROWN

The Vitamins and Allergy

ETHAN ALLAN BROWN, M.R.C.S. (LONDON), L.R.C.P. (ENGLAND), F.A.C.A.

The scientific literature which concerns itself with the vitamins can be divided into several categories. There is at first the work on the purification of those vitamins already known and their application to known vitamin deficiency conditions. There is the discovery of new vitamin fractions inherent in which is the possibility that there are previously unsuspected avitaminoses. There is the work on the effect on normal physiological processes of the presence or absence of adequate vitamin intake. Lastly as each vitamin becomes widely available and relatively inexpensive in cost, the attempt to treat diseases or conditions not known as avitaminoses and not associated with typically physiological abnormalities. An examination of the Cumulative Index for the last 15 years shows that there are few if any of the ills to which human flesh is heir to which, with no scientific basis, have not been treated with any one or all of the known vitamins.

As far as an internist interested in allergic problems is concerned the following problems must be answered. First, is sensitivity (using the word in its broadest meaning) due to any vitamin deficiency? Second, if it is not mediated by a vitamin deficiency can accessory food factors given in abundance affect the clinical course of any allergic disease? Third, can any vitamins have any effect upon any of the conditions not due to but associated with allergy although they are not direct causative factors.

It must be said at the moment that we have no clear indication that allergy in human beings can in any case be caused by a vitamin deficiency. It is possible, however, that such deficiency although not primarily important has a secondary effect. This can only be proved, unscientifically to be sure, and in the most haphazard way by watching the effect upon patients of the ingestion of large amounts of the more easily available preparations. Unfortunately many of the papers recording the effect of such work are not worth listing for the simple fact that the original conditions are not so well described; that the diagnoses are without question. Usually there are no adequate controls; the improvement reported upon is subjective in type; the vitamins are occasionally given in numbers so that the improvement if any cannot be pinned upon any special one. Many investigators did not know or lost sight of the fact that vitamin A is concerned with the metabolism of epithelial tissues arising from ectoderm and endoderm, that some of the vitamin B fractions affect ectodermal structures and vitamins C and D with mesodermal tissues and that a number of secondary factors including the presence or absence of infection, the ingestion of alcohol, the mineral intake, and the endocrine balance all may vary the response to vitamin ingestion.

Frei[14] has shown that in guinea pigs vitamin A has no significant influence upon sensitization by old arsphenamine. Groups of guinea pigs first sensitized and then tested to old arsphenamine and later placed upon very high or very low vitamin A diets reacted to the intracutaneous injections of old arsphenamine in an identical way and to the same degree as they did before their diets were changed. Other animal experimentation, however, has shown that there may be relationship between vitamin A and the sympathetic nervous system. Thiele and Guzinski[47] demonstrated that after epinephrine injections the liver became almost entirely vitamin

A free, the injection of epinephrine elevating the vitamin A level of the blood. Another possible secondary relationship between vitamin A and allergic conditions is suggested by the work of di Sant'Agnese and Larkin[7] who found that in four cases of intractable infantile eczema each was characterized by retarded development, malnutrition, marked lymphadenopathy, high blood eosinophilia, frequent severe respiratory infections and a severe generalized eczema refractory to local or dietetic treatment. An examination of the vitamin A blood levels before and after the ingestion of oleum percomorphum demonstrated that the patients had a vitamin A deficiency supposedly resulting from a defect in intestinal absorption, the authors feeling that the respiratory infection and the malnutrition were due to this fact.

In work including other vitamins with vitamin A it was shown by Kuttner[27] that large doses of vitamins A, B, C, and D had no effect upon the number of upper respiratory infections of a group of 108 rheumatic children. The weight gains of this group and the control group were essentially the same as was the response to infection. In addition a symposium arranged in 1939 under the auspices of the Council on Pharmacy and Chemistry and the Council on Foods of the American Medical Association also concluded that it had not been proven that the administration of vitamin A over and above the normal requirements conferred any exceptional immunity to respiratory disease.

The situation as far as vitamin B complex is concerned is more difficult to evaluate. The vitamin B complex includes such differing factors as thiamine, riboflavin, nicotinic acid (niacin), pyridoxin choline, biotin, panthothenic acid, Maturation factor, Gray hair preventive factor, Liver damage preventive factor, Curative factor for egg white injury and a number of other factors including factor W and factor U. The present picture of vitamin B deficiency in no way suggests any clinical syndrome typical of allergy, in human beings.

In animals Kim and Lee[24] reported that anaphylactic shock in guinea pigs could be inhibited, if vitamin B was given during the sensitization period or one hour prior to the administration of the shocking dose. Wedgewood and Grant[54] stated that rats could only be allergized when on a vitamin B deficient diet.

From the medical point of view vitamin B_1 has been used with varying success. Morehead[35] reported upon a case of chronic bronchitis and severe asthma for which immediate relief was secured with 30 mg. thiamine given intravenously with complete recovery of both conditions following six months of treatment with 3000 mg. thiamine-HCl given intravenously in doses of 30 to 40 mg. at intervals of six to eight hours at first, and later once daily the injections being supplemented with oral administration of the vitamin B complex. He also reports seven other patients similarly treated with satisfactory results. It has been stated by Shannon[42] that thiamine hydrochloride taken orally or by injection will protect patients from mosquito bites relieving the itching and eliminating formation of a papule. A dosage of 40 mg. given every four hours brought relief within twenty-four hours to ten patients who thereafter took maintenance doses as necessary. The effect of thiamine chloride on itching conditions of the skin had previously been reported upon by the same author who stated that large doses of thiamine taken orally controlled the itching associated with a number of conditions including morbilli, urticaria, eczema, scabies, pityriasis rosea, and other conditions, the doses varying from 20 to 40 mg. a day. The itching of the skin in all but six of thirty-five patients was controlled by these means.

Thiamine on the other hand has been reported as causing sensitivity. Schiff[40] in the *Journal of the American Medical Association,* described a patient who had been given several courses of intramuscular injections of thiamine for the treatment of arthritis. Given a routine dose the patient collapsed, her pulse becoming imperceptible, respiration ceasing within one minute following the injection. Arti-

ficial respiration was instituted and epinephrine 1 c.c. was given intravenously. The patient recovered. Scratch tests with aqueous and commercial solutions of thiamine hydrochloride showed positive skin-test reactions. The remaining ingredients of the solutions gave negative reactions. Passive transfer tests were negative. The shock reaction was said to have been due to an acquired sensitivity to thiamine hydrochloride.

Other cases of thiamine chloride hypersensitivity have been described. Among others one by Laws[28] and two by Eisenstadt.[11] The first a white woman aged seventy-two, received subcutaneous injections, thirty for ten days and then weekly for eight weeks and thereafter at ten-day intervals. Within thirty minutes after her last injection she developed generalized urticaria, angioneurotic edema with dyspnea, wheezing and cyanosis. Responding within a few hours to an injection of epinephrine the patient gave positive skin tests and positive passive transfer tests to the aqueous and commercial preparations of thiamine hydrochloride, a time interval of ten days having elapsed between the previous injection and the one which caused her reaction.

The patients described by Eisenstadt[11] responded, the first, with angioneurotic edema, and the second, with local swelling and itching. Both patients, however, were able to tolerate thiamine by mouth. Both gave positive skin test reactions but negative passive transfer tests.

Carlström[3] and his colleagues pointed out why some cases of vitamin B_1 deficiency failed to respond to its administration. They suggest that flooding the system with thiamine results in the binding of large amounts of pyrophosphate probably excreted in the urine. The treatment would then remain without effect until this loss of pyrophosphate was replaced since the vitamin B_1 combines in the body with the pyrophosphate to form an enzyme needed for the oxidation of pyroracemic acid. They report on seven patients who did not respond to vitamin B_1 until they were also given the pyrophosphate.

The vitamin B complex containing all the factors has been reported as affecting the course of infantile eczema. Kristensen[26] found vitamin B_1 to be ineffective but he and Vendel[50] stated the complex was "infallible" in the treatment of acute or chronic eczema. In this country, Harris and Gay[17] stated that of twenty infants, two given the vitamin B complex healed completely, eleven improved and seven showed no change.

Although migraine is not usually allergic in origin, a sufficient number of the patients desiring study for the discovery of allergenic causes remain to be treated by allergists. Of interest is a paper by Palmer[37] who treated forty-eight cases of migraine with vitamin B_1 intramuscularly supplemented by oral doses of the vitamin B complex. Twenty-three of the patients were completely relieved, some remaining free from recurrences as long as seven months after therapy had been terminated. Although 58.8 per cent of these patients reported relief from ergotamine tartrate, 70 per cent were relieved by thiamine hydrochloride. In a later series the same author stated that 75 per cent or twenty-four out of thirty-two attacks of severe migraine were interrupted within two to three hours after an intramuscular injection of 30 to 90 mg. of thiamine hydrochloride.

If it is believed that some of the patients demonstrating a typical Ménières syndrome may be allergic. It is interesting to note that Harris and Moore[18] gave thiamine chloride to twenty cases, supplementing it with nicotinic acid, seventeen of the patients becoming entirely free from vertigo and the other three presenting a marked improvement following two to three months of treatment. The dose was vitamin B_1, 20 mg. daily and nicotinic acid, 250 mg. daily.

Kalber[22] reported that in three patients with chronic bronchial asthma the subcutaneous administration of 1 mg. of vitamin B_2 (Lactoflavin) combined with 1 mg. of adenosin phosphoric acid given at intervals of from five to eight days caused great improvement. In some patients, however, there was no change.

In 1938, Madison, Fish and Frick[29] reported that nicotinic acid in massive doses augmented the production of specific precipitin antibody while small doses caused a diminution in antibody production. The effect noted was not as great as that produced by ascorbic acid.

It was shown in animal experimentation by Soldati[43] that dogs deprived of the complete vitamin B complex resisted both the bradycardiant action of injection of pitressin as well as the tachycardiant action of atropine. They reacted normally, however, to injections of acetylcholine. Of interest to the allergists, however, is that their vascular systems responded to epinephrine with a hypertensive reaction more intense than those exhibited by dogs on normal vitamin B complex containing diets.

During the same week in May, 1943, Suranyi[46] in Switzerland and Melton[34] in England published papers on the treatment of allergic conditions with nicotinic acid. Suranyi noted that the oral administration of nicotinic acid produced symptoms similar to those following the injection of histamine and therefore used the substance experimentally for patients suffering from bronchial asthma and urticaria. The dose was 0.025 to 0.05 Gm. twice daily before meals for three weeks for those patients in whom nicotinic acid orally produced an erythema. Melton gave 50 to 100 mg. of nicotinic acid intravenously to nineteen patients during one or more acute paroxysms of bronchial asthma achieving definite improvement in sixteen but marked exacerbations in two. In thirty patients who were having frequent and severe paroxysms which were not easily controlled by ephedrine, nicotinic acid was given between attacks in a 50 mg. dose two to three times daily. In sixteen of these patients the severity and frequency of the attacks were definitely reduced, relapse occurring when the ingestion of the drug was discontinued. Twelve patients given control injections of sterile water in order to make certain there was no psychological factor did not show the same response. For the patients receiving the material by mouth, control tablets of citric acid were given in which cases there were frequent relapses.

Maisel and Somkin[31] gave twenty-nine intravenous injections of .1 Gm. of nicotinic acid to twenty-one patients who were suffering severe asthmatic attacks or were in status asthmaticus. Nine patients were given 0.2 Gm. of nicotinic acid orally three times daily before meals. Their relief appeared to coincide with the appearance of a flush. None showed untoward reactions or acquired tolerance during the period they were observed. The authors felt that nicotinic acid diminished both the frequency and severity of asthmatic attacks in about 70 per cent of their patients.

Murano[36] also gave nicotinamide therapy to infants suffering from eczema. He stated that there was rapid relief from the itching and disappearance of the other skin symptoms in two to three weeks. For the first seven to ten days he gave ten centigrams intramuscularly the injection being given every other day for ten days more. Oral therapy of two to three tablets containing twenty centigrams each was given on the days on which the patient took no injection. Some of the patients manifested flushing and restlessness.

In 1939 McGinty[33] and in 1940 Doughty[8] reported on the effect of nicotinic acid upon patients receiving large doses of sulfanilamide. The first stated that the mental apathy so often present with the ingestion of sulfanilamide and that the other depressive symptoms and the porphyrinuria were decreased. Doughty reported on complete relief of headache and nausea when nicotinic acid was administered so that the administration of sulfanilamide could be continued more easily.

There are a few positive reports as to the effects of vitamin B_6 upon any allergic condition. Of interest, however, is a paper by Vilter, Aring and Spies[51] on a case of peripheral neuritis due to arsenic which could be brought into partial remission by intramuscular injections, at first, of pyridoxin alone and more spectacularly when

the patient received vitamin B_6 20 mg. and alpha-tocopheral 50 mg. intramuscularly twice daily. The patient relapsed when saline or thiamine were administered instead, or when the vitamin B_6 was discontinued. To maintain improvement, however, the vitamins had to be administered daily.

Despite the discouraging reports, work in progress with some of the other fractions of vitamin B complex suggest that they may play a part in allergic conditions. These will be reported upon in the near future.

Since it would be obviously impossible to review all of the literature concerning the relationship between vitamin C and those conditions which, in any sense of the word, may be allergic, an arbitrary limit was set and only the work done during the last five years was studied.

The evidence that vitamin C deficiency is a cause of allergization is by no means conclusive. In 1935 Sulzberger and Oser[45] reported that guinea pigs deficient in vitamin C could be sensitized to arsphenamine more readily than those which were taking normal amounts. In the following year Steinback and Klein[44] reported that animals had an increased tolerance to tuberculin when given sufficient vitamin C. In the following two or three years it was reported by Cohen[4] and also by McDonald and Johnson[32] that the presence or absence of vitamin C had no effect either upon an animal's capacity for becoming sensitized eczematogenously to arsphenamine or to poison ivy or, upon it tendency to go into anaphylactic shock. Kile and Pepple,[28] on the other hand, reported that animals showing marked signs of vitamin C deficiency could not be sensitized. In 1939, Yoshikawa[56] reported that the guinea pigs were more easily sensitized if given small quantities of vitamin C but incapable of being sensitized when given large amounts; moderate intake having no effect.

For human beings Walzer,[53] reviewing the literature, felt that the definite role for vitamin C in experimental human hypersensitivity had not yet been established and Bundeson[2] and his colleagues, reporting in the *Journal of the American Medical Association* in 1941, felt that there was no clear evidence that human allergy could be affected by vitamin C intake.

Dragstedt,[9] in 1938, set out to study the relationship between vitamin C and peptone shock in dogs. Previous workers have stated that the administration of vitamin C inhibited anaphylaxis in sensitized guinea pigs but did not protect them against histamine shock, assuming that the vitamin C prevented the liberation of histamine but could not inhibit its action after it had been liberated. Dragstedt and his colleagues discovered that the administration of vitamin C prior to the induction of peptone shock in dogs failed to prevent their reactions. He and his colleagues concluded that vitamin C does not prevent anaphylaxis by inhibiting the liberation of histamine. In the next year, however, Yokoyama[55] reported that he could prevent anaphylactic shock in sensitized guinea pigs by injecting ascorbic acid immediately before a second injection of horse serum. The reaction was also prevented if the horse serum was mixed with ascorbic acid before injection. The Schultz-Dale reaction of isolated intestine from sensitized guinea pigs was inhibited if ascorbic acid was added to the Ringer-Locke solution five minutes before adding the horse serum. A slight reaction was obtained under the same circumstances in isolated uterine strips but the author explained the slight reaction by considering the uterine muscle more sensitive than the intestinal.

Studying the effects of vitamin C upon specific precipitin production against the injection of bacterial vaccines in rabbits Madison, Fish and Frick[30] concluded that there was an increase in the precipitin production but a marked decrease in the specific agglutinins. They postulated two competitive defense mechanisms responsible for humoral immunity. One of these might be an extracellular synthesizing process and the other an intracellular lytic process. If this were true, vitamin C activation of tissue enzymes might increase the precipitin production and yet reduce the yield of specific agglutinins. It would mean that vitamin C, valuable to

the treatment of infections, would have little or no value when used as an adjuvant to vaccine therapy.

The following year Walther[52] using rabbits and also guinea pigs shocked them by the intratracheal introduction of the specific antigen of the pneumococcus. His histological study of the animals showed the presence of marked hemorrhage, emphysema and widespread distribution of eosinophilia in the alveoli, the bronchi and the interstitial tissues. The pretreatment for seven days with large amounts of vitamin C previous to the shocking injection did not decrease the local anaphylactic pulmonary response and in some cases seemed to intensify it. In the same year Ardy[1] reported that guinea pigs kept on either a high vitamin C or a low vitamin C diet showed no variation in their blood complement. In the following year Ecker[10] reported a definite correlation as existing between the ascorbic acid content and the complementary power of the blood serum of guinea pigs. He found that the complement which had been inactivated by iodine, hydrogen peroxide, quinine and iodoacetate could be reactivated with various reducing agents as ascorbic acid, hydrogen sulphide and potassium cyanide. Complement taken, however, from anaphylactic animals could not be reactivated in the same way.

Freidman[15] studied the contractile response of the isolated smooth muscle of the guinea pig to stimulation with histamine under conditions of vitamin C deficiency and adequate diet. In the isolated smooth muscle preparations of the animals suffering from scurvy the minimal stimulating dose of histamine was at least one thousand times as great as that in the control group, the diminution in contractile response developing after the animals had been on the scorbutogenic diet for three or four days, remaining constant up to thirty-five days.

Ruskin[39] devised an ingenious experiment by which the direct effects of drugs could be studied by microscopic examinations of the rabbits' bronchioles. Histamine was applied to produce broncho-constriction and then drugs antagonistic to histamine applied to the constricted bronchioles. After relaxation of the bronchioles by the drugs antagonistic to histamine a second addition of histamine caused a little secondary contraction. Ascorbic acid and sodium ascorbate when used in this manner relaxed the bronchioles but inhibited the constricting effect of the second addition of histamine. When ascorbic acid was added as an acid radical to calcium, ephedrine, benzedrine and epinephrine the ascorbate counteracted the histamine effect although the original compounds which did not contain the ascorbic acid radical promoted histamine activity. Ruskin reported epinephrine ascorbate as antagonizing histamine more quickly and more actively than epinephrine hydrochloride, having twice its bronchodilation capacity. He felt also that there was a relationship between the physiological activity of calcium and histamine and that in the presence of a vitamin C deficiency calcium might definitely be contraindicated in histamine shock.

In a similar experiment Farmer and Kassman[12] dealing with serum-sensitized guinea pigs kept on an ascorbic acid-deficient diet for six to nine days stated that there was no increase of anaphylactic response. Normal guinea pigs kept on an ascorbic acid-deficient diet for the same length of time showed a slight increase in histamine sensitivity. An examination of the ascorbic acid content of the adrenals of the normal guinea pigs kept on an ascorbic acid-deficient diet for seven days showed only a moderate decrease in the amount of ascorbic acid present. The authors felt that the anaphylactic response in the histamine sensitivity depended upon the degree of ascorbic acid depletion of the adrenal glands.

It was not long after the work mentioned above was published that vitamin C was given to human beings suffering from allergic complaints. Studies by Goldsmith, Ogaard and Gowe[16] on thirty-two allergic patients showed that twenty-nine had subnormal levels of ascorbic acid and only three had adequate vitamin C nutrition whereas forty-three control patients presented normal blood vitamin C

levels. Seven patients with bronchial asthma, one with hay fever and one with urticaria were given standardized diets in order to determine whether or not allergic patients required more vitamin C than did normal control individuals. The authors concluded that six of the seven patients with asthma were unable to maintain as high a level of blood ascorbic acid as could a control group under the same regime. In two of the patients the frequency and severity of asthmatic attacks were reduced but, in the other five, the condition was unaffected following saturation of the body with ascorbic acid. These results were not surprising since Hunt[20] had shown three years previously that doses of 100 mg. daily of ascorbic acid had had no effect whatsoever in a group of patients with bronchial asthma.

In five out of seven cases with previous arsphenamine dermatitis Cormia[5] showed that massive intravenous doses of vitamin C with high oral maintenance doses enabled the patients to tolerate the drug. Attempts, however, to sensitize those patients who showed low vitamin C levels, by the intradermal injection of neoarsphenamine failed in every case. Cormia concluded that vitamin C was probably related to arsphenamine sensitization but postulated an X factor necessary for the production of cutaneous sensitivity. This work was corroborated by Delp and Weber[6] in their study of vitamin C levels in one hundred and six patients with untreated syphilis showing that these were in direct proportion to the dietary intake of the vitamin. Groups of patients who had been given treatment with the heavy metals showed no change in the vitamin C values. The authors favored the treatment of arsenical dermatitis with cevitamic acid suggesting that such therapy would warrant further study. Vail[49] on the other hand reported that arsenical sensitivity was most commonly associated with a vitamin C deficiency although in a small percentage of cases reactions could occur although the blood vitamin C values were normal. He felt that the best results were obtained by intravenous therapy although oral administration of vitamin C was effective, the symptoms of arsenical sensitivity disappearing as the blood vitamin C increased, the best results occurring in those patients who took small doses of vitamin C at the same time they had their arsenical medication.

Large amounts of vitamin C were soon given to patients with hay fever. Holmes [19] in five patients gave 100 mg. daily for one week in twelve patients 200 mg. doses and in some patients 5 mg. daily, reporting almost complete relief after two to four doses of 500 mg. in all but three patients who completed the treatment. One patient with bronchial asthma was greatly relieved following 500 mg. doses daily for two weeks and a female patient almost completely cured of eczema after 150 mg. daily for one month. One patient responded with a toxic reaction, presenting a rash. Korbsch[25] had reported, five years previously, that doses of ascorbic acid up to 1 gram daily by mouth relieved a number of patients suffering from allergic coryza, serum rashes and erythema multiforme.

More recently Pelner[38] prevented the toxic reaction from which a patient had suffered following the use of sulfathiazole by giving him 100 mg. of ascorbic acid with each dose of sulfadiazine. He treated in all, fifty-one patients none of whom showed the usual depression seen after sulfonamide therapy when they were given vitamin C at the same time.

Considering the extent of our knowledge regarding the inter-relationship of calcium and vitamin C it is indeed, surprising that none of the authors listed above excepting Ruskin mentioned this fact although there are many reasons for believing that such an inter-relationship exists. Work in progress and timed for publication in the near future and in the present review will attempt to correlate some of the relationships between the vitamins and minerals in normal metabolism. The inclusion of such work at this time

would make the present paper too unwieldy for everyday reference and use.

The present paper represents only a brief résumé of some of the contemporary work on vitamin deficiencies and allergy. When it is seen that there have been over ten thousand papers written on the forty or more known accessory food factors it can be understood how impossible it must be to treat the subject adequately. In the limited space at our disposal only an arbitrary period of time (five years) could be reviewed and only the more important papers in the field given study. Future papers in this series will attempt to fill in some of the more obvious lacunæ.

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ALLERGIC REACTION TO DRIED HUMAN PLASMA. Colonnell, William J., Lt. Commander, MC, USNR: U. S. Naval M. Bulletin, 11:1356, (Sept. 1943.

The patient, who had had two whole blood transfusions from one donor, had urticara following the second transfusion. The recipient had no personal nor familial history of allergy. The donor was sensitive to ragweed pollen. Following the transfusion, the recipient showed a 3-plus reaction to ragweed pollen, and also a 1-plus to the same activated plasma (Dilution 1:10) used in transfusion. The presence of ragweed allergen in pooled human plasma was demonstrated in passive transfer on three control patients. The third transfusion gave the recipient: angioneurotic edema; asthma and urticaria.

L. J. H.

MILK INTOLERANCE, THE CAUSE OF A NUTRITIONAL ENTITY. A Clinical Study. McClendon, P. A., and Jaeger D.S.: Southern M. J., 36: 571, (Aug.) 1943.

The authors base their observations upon sixty-five private patients seen during the last five years. In order of frequency, the milk intolerance showed itself by complaints of: constipation, anorexia, abdominal pain, abdominal distress, a sense of fullness, pallor, fatigue, irritability, recurring diarrhea, repeated colds, asthmatic bronchitis, enuresis, and urinary frequency. The degree of intolerance was variable. The patients' histories showed a familial allergy, and excessive ingestion of milk by their mothers during the period of gestation. Each patient followed an identical pattern in each instance. The physical examination showed the patients to have the characteristics of poor nutrition. Case Reports.

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Allergy in Otolaryngology and Ophthalmology

A Review of the Recent Current Literature

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A review of the literature on the subject of allergy in relation to otolaryngology for the year 1943 shows distinct advances in this special field. Progress, however, seems very slow for there should be many more papers than those presented. There is certainly a great deal of need for further investigation in this field and there should be close coöperation with the allergist. During the past twenty years attention has been called repeatedly to the importance of allergy in its relation to nasal and sinus diseases and yet many otolaryngologists pay little attention to it. Far too many patients with nasal allergy are treated for frequent colds and sinusitis and too many tonsillectomies are performed on children who have unrecognized respiratory allergy. Few ever take the trouble to make a cytologic examination of the nasal secretion. It is true that many otolaryngologists are too busy to spend additional time on allergy patients. Most of them do not have an adequate working knowledge of the subject. Nevertheless, it is the duty of every otolaryngologist to make some provision for the treatment of these patients. Similar conditions exist in the field of pediatrics, particularly in the management of respiratory allergy.

Although this situation appears discouraging, there is now a greater movement on the part of the national allergy organizations to promote the knowledge of allergy in other fields and to bring together all allergists and specialists in an effort to produce closer coöperation.

PHYSIOLOGY AND PATHOLOGY

Fowler[12] reports an interseting case of a woman thirty-four years of age who developed a typical Horner syndrome on the left side following removal of the left stellate ganglion for the relief of pain in the left arm. Obstruction and profuse watery discharge appeared on the left side of the nose. Smears of the nasal secretion from this side showed eosinophiles. Skin tests were negative. The symptoms were controlled with syntropan. Among four other patients with Horner's syndrome, one had symptoms similar to the above patient. It was not stated whether eosinophiles were demonstrated in the nasal mucus in this case.

Mohun[26] reported a group of eight cases in which nasal blocking or congestion developed during pregnancy in women who had never had such symptoms when not pregnant. Five of these women had had similar symptoms during one or more previous pregnancies. The symptoms disappeared within one to seven days after delivery.

In another group of twelve women who already had hay fever or nasal allergy, the symptoms were markedly increased during pregnancy. Mohun concludes that the increase in estrogen during pregnancy is probably the etiologic factor.

Unilateral polyposis not infrequently occurs in older children and adolescents. dos Reis and Corrêa[8] report their observations on a group of seven cases. The patients varied in age from twelve to twenty-one years, most of them being in adolescence. The Caldwell-Luc operation was successfully performed on all of them. This type of polyp is usually presented in the choana, the attachment being most frequently in the antrum. It is important to differentiate this type of polyp from that of allergic origin. The choanal polyp is not the result of allergy; therefore, it should not be erroneously treated as such.

A most outstanding contribution has been made by Hilding[16] on the relation of ciliary insufficiency to death from asthma and other respiratory diseases. He points

out that there is a group of cases among patients who die from asthma who show a very striking and characteristic change in the bronchial epithelium. The change consists of a substitution of goblet like cells for the normal columnar ciliated cells. Apparently it is a true metamorphosis. As this change takes place, the ciliary mechanism is lost and the characteristic viscid, mucinous secretion accumulates in the air passages. Normally this viscid secretion is very readily carried up vertical surfaces by ciliary action. The amount of secretion is enhanced because the erstwhile ciliary cells are secreting as well as the glands. The difficulty of removal of the secretion is aggravated because the mucin remains attached over large areas within the cells which produce it, thus anchoring the mass to the wall. When the air passages have become completely filled, the patient dies of asphyxia. In Hilding's opinion, this metamorphosis is the chief pathologic change and death results directly from the loss of ciliary function.

He noted a second group of asthmatics in which the cilia were also lost, but the picture was essentially different. This group was characterized by chronic bronchitis with purulent secretion. There was destruction in the surface of the bronchial epithelium and the ciliated cells had sloughed off very extensively. In these patients also the air passages filled up with secretion to such an extent that the patients died. Attention is also called to the fact that bronchospasm was doubtless a factor in some of these cases. In one of the group which was omitted from this discussion, spasm seemed to play a dominant rôle. A patient with tracheobronchitis who died in extreme respiratory distress showed the ciliated epithelium was practically entirely destroyed and all the bronchi contained viscid plugs of secretion. Further studies were conducted on pathologic material from the pandemic of influenza in 1918. The material was not entirely satisfactory, but as fas as could be determined the bronchiolar epithelium had been entirely destroyed and all the cilia with it.

In all of these groups, Hilding feels that the mechanical removal of the secretion as a substitute for ciliary action is indicated. Aspiration, either through a bronchoscope or a tracheotomy, would be the best.

In a series of animal experiments, Hilding[17] has shown that certain pathologic conditions in the upper and lower respiratory tracts, such as postoperative pulmonary atelectasis, vacuum headache and retraction of the ear drum, are the result of insufficiency of ciliary activity.

The steps in the development of postoperative pulmonary atelectasis were outlined as follows:

"(1) An excess of secretion is formed within the affected lobe. (2) A succession of occluding masses, or pistons, of mucus form across the lumina of the air passages. (3) These 'pistons' move up the cylindrical air passages by ciliary action, each carrying a quantity of air. (4) As soon as the pressure within the lobe begins to fall, it shrinks by its own elasticity and from pressure by adjacent lobes. (5) The adjacent lobes carried by the force of inspired air move into the space relinquished by the affected one. (6) The advancing pistons rupture serially as they reach tubes of greater diameter and meet more forceful changes of air pressure. Each then releases the bubble of air which is carried and continues on its course as a mural mass of film. (7) A negative pressure of considerable proportion is produced within the lobe when the supply of air is exhausted. (8) The masses of secretion then present in the air passages come to a standstill when the cilia can no longer advance them against atmospheric pressure. (9) The cilia continue to remove secretion from these stalled masses in thin films and might eventually remove them entirely if they were not replaced by continued secretion."

In the experiments regarding vacuum headache, he noted that negative pressure can be produced within a normal sinus by the introduction of a quantity of mucus which replaces a portion of the contained air. When the ostium becomes occluded negative pressure develops within the sinus. The pressure falls as the mucus passes through the ostium. The pressure ceases to fall when it becomes equalized on the

inside and the outside. The cilia continue to act and remove the mucus in thin films. When sufficient mucus has been removed, atmospheric pressure forces air into the sinus again. In this manner, Hilding states, negative pressure almost certainly develops clinically in sinuses more or less filled with mucus.

The negative pressure which is known to occur in the middle ear is probably caused by the force of ciliary action moving mucus down the eustachian tube.

DUSTS AND MOLDS

In a group of 100 selected patients, Davidson[5] noted that of ninety-five reacting to house dust, ninety also reacted to animal hairs. In this group he felt that animal hairs were responsible for the production of symptoms in only 10 per cent. This brought up the question as to whether the animal hairs contacted in other ways than from live animals were responsible for the activity of house dusts. On the basis of clinical observation and skin tests, Davidson concludes that the final proof of the constitution of house dust awaits the development of tests by which to differentiate the almost endless number of allergens in it. Some investigators have presupposed the presence of some unknown ingredients in house dust which would account for its activity. He finally concludes that house dust is composed principally of cotton, flax, jute, wool, silk, six or more animal hairs, three or more feathers, glue, kapok, orris root, pyrethrum and tobacco.

Durham[9] has presented a very comprehensive treatise of the subject of air-borne fungus spores as allergens. His report is based upon extensive observations made in the United States, Alaska and some foreign countries. A comparative study of the total seasonal fall of alternaria and hormodendrum spores and ragweed was made in fifty-three cities. In number and in widespread geographic distribution, the spores of stem rust, alternaria and hormodendrum are outstanding. The daily fluctuations of mold spore concentrations are more pronounced than those of pollen and are not as easily accounted for by weather conditions as are fluctuations in the pollen curve.

The importance of these air-borne fungus spores as a cause of allergic conjunctivitis, nasal allergy and asthma cannot be too strongly emphasized. In the central states area we have found them to be the cause of respiratory allergy during the spring, summer and early fall, in a significant number of cases. These patients may or may not be sensitive to pollen; as a rule they are not, but have been considered as pollen-sensitive by a number of observers. In most instances, however, skin reactions to pollen were considered as borderline or negative. In the diagnosis and treatment of these cases we have employed an extract of feed-mill dust such as that described by Wittich.[35,36] This dust contains all the spores noted on slides exposed for making the pollen counts. Positive skin reactions to this extract have been consistent, and treatment with small doses has resulted in most satisfactory relief. In a number of cases presenting a rather typical history of the vernal type of conjunctivitis, the response to mold therapy was also satisfactory.

ALLERGY AND PEDIATRICS

Clinical papers on allergy in children by Deamer,[7] Long,[20] Criep,[4] Miller[25] and Marks[21] emphasize the importance of the diagnosis and treatment of respiratory allergy. Attention is called to the fact that symptoms simulating the common cold, characterized by sneezing, nasal obstruction and discharge are frequently overlooked as allergy and treated as infection. There should be no difficulty in making the distinction between allergy and infection if the nasal secretions are examined for the presence of eosinophiles or neutrophiles. It is important to consider the common cold, however, as a complication of a nasal allergy. During a cold there may be an absence of eosinophiles. Follow-up examinations in these cases will reveal an eosinophilia after the cold has subsided. Some of these observers call

attention to the frequent unnecessary removal of tonsils and adenoids in these cases considered as infections. Chronic persistent cough in children is often a forerunner of asthma and should be carefully investigated from the allergic standpoint.

THE NOSE AND PARANASAL SINUSES

Shambaugh[31] reports his observations on the differentiation of infectious and allergic rhinitis. In 102 consecutive cases of chronic nasal or sinal disease which he reviewed, the condition was essentially nasal with secondary involvement of the sinuses in fifty-one. In forty-three of these there was response to allergic treatment. In the other fifty-one cases the disturbance was primarily sinal and in thirty-six of these a response to treatment for allergy was obtained. He emphasizes that both the infection and the allergic condition must be treated in order to give maximum relief.

In the management of allergy as related to otolaryngology, Hansel[15] emphasizes the importance of diagnosis of nasal and sinus allergy as well as other associated manifestations. In the treatment of hay fever small doses of pollen extracts given subcutaneously or intracutaneously are recommended. Both preseasonal and coseasonal methods may be employed. In the treatment of dust sensitives, small doses are also recommended, starting with a 1-10,000,000 dilution in small children, 1-1,000,000 in older children and in adults with severe symptoms. Most patients received satisfactory relief with maximum doses of .10 to .20 of 1-100,000 or .10 to .20 of 10,000. In only a few cases was a 1-1,000 dilution employed. On the whole, the skin tests as a means of determining the relative degree of sensitivity to dust was found unreliable. Very good results were obtained in cases in which the skin reaction was entirely negative. In general, the administration of weak or stronger doses was based upon the degree of clinical sensitivity or severity of symptoms. Weak dosage was employed in the severe cases and stronger dosage in the mild cases.

In the study of cases of so-called recurring sinusitis, bronchitis, colds or catarrh in Southern California, Smith, Goodhill and Webb[32] point out that such conditions are caused by an unrecognized or hidden pollen allergy. The pollen allergy problem in Southern California presents great difficulties owing to perennial pollen present in the air. They state that continual exposure to perennial pollens results in the development of a low-grade resistance which is not sufficient to prevent allergic symptoms but does result in minimum reactions to the usual skin tests. Perennial pollen treatment, including empirical treatment with the pollens indicated by the patient's history and environment when tests were inconclusive, was found to be of definite value.

In the diagnosis of pollen allergy, the skin reaction is considered a very reliable guide. Minimal or borderline reactions always present a problem in treatment. It is important to take into consideration the possibility of atmospheric mold sensitivity in those cases. If the patient's symptoms parallel the pollen count, treat with pollen extracts. If they parallel the atmospheric mold count, treat with molds. In some instances treatment with both may be indicated. According to our experience in the central states area, therefore, most of the questionable pollen cases have proved to be mold cases.

In a group of eighty cases of chronic maxillary sinusitis in which an antrum window operation was performed, McHenry[23] reports that in twenty-one the infection was of dental origin and in twenty-three allergy was a factor. Among the allergy cases, eighteen were relieved of their sinus symptoms. In the entire group of eighty cases, sixty were considered as cured, twelve were relieved of symptoms, and in eight the results were unsatisfactory.

In a personal study of 250 patients who had had operations on the nose and sinuses, Hollender[18] found that the results were satisfactory in 65 per cent of the

nasal cases and in 38 per cent of the sinus cases. According to the results reported by 154 rhinologists in a reply to a questionnaire, the "cures" reported were 71 per cent for nasal surgery and 42 per cent for sinus surgery. Hollender finally concludes that the chief factors in unsuccessful operations are: inaccurate diagnosis; neglect of allergic factor; failure to appreciate the importance of systemic diseases, such as diabetes, syphilis or tuberculosis; too hasty surgical intervention; poor surgical technique or incomplete operations; and inadequate postoperative care.

According to the observations of Urbach and Gottlieb,[33] vasomotor rhinitis was encountered in 38 per cent of 379 cases of asthma. This percentage seems far too low. In children with asthma we found the incidence of nasal allergy almost 100 per cent. In adults with asthma, the incidence of nasal allergy is about 90 per cent. These estimates were corroborated by positive cytologic findings in the nasal secretions. Nasal allergy associated with asthma is often very mild, so much so that the patient does not complain about it, yet a diagnostic eosinophilia is present.

After fourteen years' study of nose and throat problems in relation to asthma, Weille[34] concludes that the rhinologist cures asthma in about 10 per cent of the cases referred to him. Symptoms are relieved in about 40 per cent for shorter or longer periods of time and no results are obtained in the remaining 50 per cent. The cases seen by the rhinologist, he states, represent the failures of the allergist to a great extent and are therefore a special group. For better results, a closer collaboration between the rhinologist and the allergist and a better understanding of the relation of sinusitis to asthma is advocated.

DRUGS

During the past few years a number of synthetic ephedrine-like drugs have been developed for the treatment of respiratory allergy. In general, an attempt has been made to eliminate those factors which cause a rise in blood pressure, palpitation and nervousness.

Friedman and Cohen,[13] in reporting the use of a new synthetic ephedrine-like drug—nethamine—in the treatment of hay fever and asthma, state that of twenty-three cases of hay fever, fourteen were improved, and of twenty-three cases of asthma eleven or 48 per cent were improved. The incidence of such symptoms as nervousness and insomnia was definitely less with nethamine than with ephedrine, while nethamine was at least equally as effective in relieving symptoms. The heart rate and blood pressure were unaffected.

Fabricant and Van[11] report their observations of the use of privine hydrochloride, a new imidazoline derivative, 2 naphthyl-methyl imidazoline. It is crystalline and readily soluble in water or normal saline. In animal experiments it was found that a 0.1 per cent solution had no detrimental effect on ciliary activity. In normal subjects it caused no alteration in the pH of the secretions. It caused no irritation of the mucous membranes or any of the toxic side-effects as sometimes noted with ephedrine.

Scott[30] reports two cases, both in children, in which severe reactions to ephedrine occurred, although both patients had been treated previously with ephedrine without ill effects. One patient, a girl aged twelve years, had used a nasal spray of 2 per cent ephedrine and had also taken it internally without ill effects. Later, following the use of 1 per cent ephedrine in the nose, she developd a severe reaction of chilliness, dryness of the throat, palpitation and restlessness. The second patient, a boy aged six years, who had hay fever and asthma, had taken ephedrine internally in doses up to ⅜ gr. with ¾ gr. amytal without ill effect. Later, during an acute infection with asthma, the same dosage was followed by a severe reaction characterized by restlessness, anxiety, thirst, rapid pulse and respiration. Scott stated that such violent reactions to ephedrine in children normally tolerant to the drug seem inexplicable, but point out the necessity for caution in the administration of ephedrine.

Although the above reactions to ephedrine might be considered of an allergic nature, it also appears that they may simply have been the result of overdosage. A dosage of 3/8 of a grain of ephedrine is very large for a child; even many adults will not tolerate it. In general, an average dose of 1/8 gr. for a child and 1/4 gr. for an adult is sufficient. In some instances large doses are required for effectiveness and may be well tolerated.

Girling[14] reports his observations on the use of histamine in 120 cases which included seventy-three cases with postnasal drip with other evidence of allergy such as intermittent nasal obstruction; fourteen cases of nasal allergy with conductive deafness; twenty cases of lower half headache with nasal symptoms; six cases of asthma; five cases of dermatitis and two cases of laryngitis. Intracutaneous tests were made with 0.01 c.c. of a 1-100,000 dilution of histamine diphosphate. An area of erythema over 35 mm. in diameter was considered a positive reaction. In the treatment of positive reactors, the dilutions used were: 1-100,000, 1-75,000, 1-50,000, 1-25,000 and 1-10,000. When the first evidence of reaction appeared, the dosage used was reduced to two-thirds of the last dose; this was further reduced if reaction continued. From twenty-five to forty treatments were given. After the course of treatment, the skin reactions were greatly reduced or negative. Of seventy-three cases of nasal allergy, seventy were completely relieved; of the fourteen cases of nasal allergy with conductive deafness, five were completely and eight partially relieved; fifteen of twenty lower half headache cases were entirely relieved; of six cases of asthma, five were completely relieved. Four of five cases of dermatitis were relieved. Both of the cases of laryngitis were completely relieved. Girling concludes that it remains to be determined whether these results are permanent.

Criep[3] reports the case of an allergic patient who developed nasal allergy and asthma following the topical application of argyrol. A positive scratch reaction was noted with a 1 per cent solution. An intracutaneous test with this solution resulted in a severe local and a mild constitutional reaction. Ophthalmic and passive transfer tests were also positive. Tests with several other preparations of mild silver protein were negative. The protein molecule associated with the argyrol was believed to be the sensitizing factor. Criep is of the opinion that argyrol may be a frequent cause of sensitization and may be the cause of the discomfort some patients experience from its use.

Kauvar and Mont[19] report their observations on a study of 127 patients with common colds, of whom seventy-five were treated symptomatically and fifty-two with sulfonamides. The usual dosage of the sulfonamides was 2 gm. initially followed by another 2 gms. in two hours, then 1 gm. every four hours. Treatment was continued from three to eight days. No complications were noted. The sulfonamide-treated patients averaged 5.01 days and the control group 5.26 days in the hospital. From these studies it was concluded that the use of sulfonamides in the treatment of mild upper respiratory infections is not justified. Toxic reactions or sensitivity may develop, thus possibly making it impossible to use in the case of the development of a more serious illness. They recommend the use of sulfonamides, therefore, only in the complicated cold cases.

Recent reports on the use of the sulfonamide drugs locally or generally in the treatment of the common cold have been controversial as to whether they are or are not effective. Davis[6] reports his observations on the treatment of 157 cases treated by ordinary symptomatic drugs and compares the results with a group of 162 in which sulfathiazole was given orally in 1 gm. initial doses followed by 1/2 gm. every four hours. A control group consisted of 187 men and women. Treatment was given for three days. At the end of that period 70.3 per cent of those given sulfathiazole were cured and 22.3 per cent were improved. Thirty-nine per cent of those given symptomatic treatment were cured, 35 per cent improved. Of the control group, 47 per cent were cured and 29 per cent improved. The 162 treated with

sulfathiazole lost thirteen days from work while in the control group of 187 ninety-six days were lost. There were a few reactions to sulfathiazole, such as nausea, eight cases; headache, five cases; dizziness, five cases. Davis concludes from this study that sulfathiazole treatment of common colds in industrial workers results in an important saving of working time.

Ebert[10] reports his results in the treatment of acute rhinitis in ninety-two patients from the use of sulfathiazole powder insufflated into each nostril daily or every other day. Relief of symptoms was almost instant and there was no irritation. The amount of sulfathiazole powder insufflated with each treatment averaged 0.0164 gms. for each side of the nose. Each patient received an average of three and one-half treatments so the total amount of drug used was only 0.12 gm. None of the patients showed the slightest toxic effect.

Our experience in the use of sulfathiazole in the treatment of the common cold is in agreement with that of Davis and of Ebert. The treatment is more effective when used early, that is, the first or second day. It should be administered about three times a day and should not be continued more than three or four days. Continued use for longer periods seemed to set up a great deal of irritation in some cases. Overtreatment might induce local and perhaps general sensitization. A great deal of caution should be exercised in treating allergic patients with colds because of possible sensitization. If a patient has had previous toxic or sensitization manifestations from the administration of sulfonamides, it should not be used in the nose, for even the small amounts introduced can cause toxic symptoms and allergic manifestations, especially dermatitis.

THE EAR

Merica[24] discusses his findings in 135 cases of vertigo due to tubal obstruction. Many of the patients had associated acute or chronic disease of the sinuses or ears. In fifteen instances the condition was associated with colds. Some patients obtained immediate relief from severe vertigo after inflation of the eustachian tubes. Some patients derived permanent relief from one inflation. Others had recurrence of symptoms and required repeated treatments. Some patients with eustachian tube obstruction proved to be allergic and improved when the offending allergen was recognized and eliminated. Patients with a low metabolic rate had improved tubal patency after the administration of thyroid.

Noun[28] reports the occurrence of chronic otorrhea caused by food sensitivity in two children, aged eight and fifteen years. Positive skin reactions were demonstrated with several foods by direct and transfer tests and were corroborated clinically. The otorrhea subsided following the avoidance of the offending foods. Re-introduction of the foods caused an exacerbation of the otorrhea. It was suggested that the membranes of the middle ear were the site of the allergic reactions. In both patients a perforation of the ear drum had existed from a previous otitis media. No cytologic studies were made on the discharge from the ears. Both children had nasal allergy.

Although it is possible that the middle ear may be the site of an allergic reaction, in cases of the type reported in which there is an old perforation of the drum associated with a nasal allergy, it is difficult to determine whether the secretion in the middle ear arises from this site or comes from the nose as a result of blowing. With the subsidence of the nasal allergy the aural discharge should also subside. We have observed a number of cases of this type in which an otorrhea subsided under similar conditions. The discontinuation of nose blowing may also result in improvement or cure.

THE EYE

Bab[1] reports his observations on allergy of the eye in a group of eighty-three cases, in forty-one of which there was edema of the eyelids. The etiologic agents

varied greatly and included sleeping pills (phanadorm) in one case; stewed cherries in another; strawberries in two others; and mechanical irritation such as that produced by plucking the eyebrows, squeezing the margin of the lid to straighten the lashes and dyeing the eyebrows.

O'Brien and Allen[29] report their observations on the diagnosis and treatment of allergic keratoconjunctivitis. This condition is characterized by recurring attacks of redness and swelling of the eyelids, accompanied by itching, lacrimation and discharge. A local eosinophilia, they state, may or may not be demonstrated. In one of the cases reported orange was the offending allergen. A patch test with orange peel was positive and the ingestion of orange was followed by keratoconjunctivitis. In another case butyn was the cause. In three additional cases the causes were hydrous wool fat in an ophthalmic ointment, a proprietary inhalant, and a fur coat, respectively.

Morrison[27] reports a case of chronic catarrhal conjunctivitis aggravated by the application of an ointment of sodium sulfathiazole and sudfathiazole. Discontinuance of its use resulted in a remission and re-application caused an exacerbation. The base was found to be inocuous.

Marton[22] reports four cases of severe vernal conjunctivitis caused by pollen sensitivity. None of the patients had nasal symptoms. Two patients failed to show reactions to pollen. One reacted to grass and ragweed and one to grass, hickory and faintly to ragweed. All four patients were given intensive treatment with pollen extracts with good results.

In cases of this type it is important to consider atmospheric molds as a possible factor.

Brown, Irons and Rosenthal[2] made the observation that workers in laboratories producing cultures of tubercle bacilli noticed that systemic reactions resulted when the fumes from boiling suspensions of dead tubercle bacilli were inhaled. After repeated exposures, cutaneous sensitivity to tuberculin became markedly decreased. In two cases reported, recurrent tuberculous iritis had been present for many years. In neither patient could foci of infection be found. Both reacted strongly to Mantoux tests. Both patients became free of symptoms after repeated inhalation of the fumes from boiling suspensions of tubercle bacilli. A slight recurrence of iritis once followed the direct exposure of the eyes to the fumes. Animal experiments showed that sensitized guinea pigs could be desensitized by the repeated inhalation of the fumes.

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Correspondence Items

Contact Dermatitis Due to Permanent Wave Process
Additional Notes

Dr. Ralph Bowen reported in the January-February ANNALS three patients with contact dermatitis due to a "cold" or "heatless" permanent hair wave process. Since that time, Dr. Bowen received the following information from Dr. Louis Schwartz, Medical Director and Chief of the Dermatoses Section of the U. S. Public Health Service, concerning cold wave solution:

According to a letter received by Dr. Schwartz from the National Mineral Company of 2628-58 North Pulaski Road, Chicago, Cold Wave Solution is made with "ammonium salt of thioglycolic acid as the essential ingredient. The compound is of a high state of purity and is accurately controlled to a pH of 9.4 with ammonia. The concentration of the thioglycolic acid proper is 6½ per cent."

Dr. Schwartz comments: "From this information, dermatitis from the Cold Wave Solution may be produced either by the fact that it is alkaline or by sensitization to thioglycolic acid. The latter is more tenable because of the fact that your patients had no difficulty on the first application but developed a violent dermatitis on the second. They became sensitized by the first application." Dr. Schwartz states that a proper dermatological study advocated by his Section when testing such products is to do patch testing on 200 individuals and ten days after removal of the first series of patches, retest them to see if any have been sensitized. The person performing and interpreting such patch tests should be an experienced dermatologist.

If there are any more cases of dermatitis of this nature, THE ANNALS would be pleased to have comments for publication.

Allergic Bronchitis

To the Editor:

In enjoyed reading the article on "Allergic Bronchitis" by Thomas and Taylor.* My interest was attracted to the statement in their summary that "Physical examination is not diagnostic, nor are laboratory procedures . . . ." I trust that their omission of mention of studies of the sputum for eosinophiles was an oversight. The differential diagnosis of chronic cough may often be difficult and it is fortunate that our armamentarium includes a laboratory procedure as simple and as informative as the examination for sputum eosinophilia. This allows us in most cases to make the diagnosis of allergic bronchitis with precision, rather than by exclusion. In the investigation of all suspected allergic disease of the respiratory tract, this diagnostic procedure should be a part of the routine examination.

With best regards, I am,

Sincerely,

ALBERT R. ZOSS, Captain, M.C.

*See page 185, November-December 1943 issue

✶ *In Memoriam* ✶

WARREN TAYLOR VAUGHAN, M.D.

Dr. Warren Taylor Vaughan died suddenly April 2, 1944, in Richmond, Virginia, a victim of coronary occlusion. He was born in Ann Arbor, Michigan, on February 22, 1893, the son of the late Dora Catherine (Taylor) Vaughan and Victor Clarence Vaughan, who was well known in the field of immunology and was Dean of the Medical School of the University of Michigan from 1891 to 1921.

Warren Taylor Vaughan received the following degrees from the University of Michigan: B.A. in 1913, M.D. in 1916, and honorary M.S. in 1941. On June 21, 1917, he was married to Emma Elizabeth Heath, and they had four sons, Victor, Clarence III, Warren Taylor, John Heath, and David DuPuy. He was house officer of the Peter Bent Brigham Hospital, Boston, 1916-17; assistant in preventive medicine and hygiene, Harvard Medical School, 1919-20. After 1920 he was in the practice of internal medicine and specialized in allergy; he was also director of the Vaughan-Graham Clinic in Richmond, Virginia. During World War I he served as 1st Lieutenant and advanced through the grades to Lieutenant Colonel, U. S. Army, Chief of Medical Service, Camp Hospital 41, A.E.F.

Dr. Vaughan also held important positions on various committees dealing with national problems; the organizations of which he was a member included the following: Fellow A.A.A.S. (council since 1938), member Medical Society of Virginia (vice president, 1931-32), Southern Medical Association, American Medical Association, American Society of Clinical Pathologists, American Association for the Study of Allergy (secretary-treasurer, 1928-38; president, 1939), Society for the Study of Asthma and Allied Conditions (president, 1938-39), American Rheumatism Association, Society of Investigative Dermatology, International Society of Gastro-enterology, Institute of Practice of Medicine, Barcelona, Spain (honorary), Society for the Study of Allergy, Argentine (honorary), Virginia Academy of Science.

Dr. Vaughan contributed much to medical knowledge and to the advancement of the subject of allergy. He was the author of several books, including Influenza, An Epidemiologic Study, 1921; Allergy and Applied Immunology, 1931; Practice of Allergy, 1939; Primer of Allergy, 1939; Strange Malady, 1941. Editorial positions included editor-in-chief, *Journal of Laboratory and Clinical Medicine;* associate editor, *Journal of Allergy,* until January 1, 1944; membership on the editorial board of the *American Journal of Digestive Diseases and Nutrition, American Journal of Clinical Pathology.* Formerly, he was a member of the editorial board of *Review of Gastro-enterology, American Journal of Syphilis,* and collaborating editor *Folia Clinica Chimica et Microscopica* (Bologna, Italy). He also contributed more than 150 articles to current medical literature, including the Encyclopedia Americana and Oxford Medicine.

More specific contributions to the subject of allergy included studies in food allergy, particularly as related to the leukopenic index and genetic classification of foods. His Practice of Allergy is appreciated by all men interested in allergy as one of the outstanding texts and reference books and in itself may be considered an encyclopedia. Dr. Vaughan was an untiring clinician and investigator. His opinion on all subjects related to allergy has been respected, and his efforts for the advancement of this subject have been unlimited. The patient understanding and aid of his wife in assisting him with many of his manuscripts as well as in his investigative work enabled him to accomplish much that otherwise would have been more difficult. His work as a teacher as well as his appreciation for the

advancement of allergy is evidenced by the number of men that he trained at his clinic in the specialty of allergy and in the time he devoted to the teaching of technicians. He ingeniously applied his hobby of photography to demonstrations of his clinical cases and in his scientific publications.

In all personal relationships, Dr. Vaughan was stimulating; he thought straight. He was original, practical, and scientific in his approach to all new problems. Under pressure he was efficient, ingenious, and resourceful—a leader and an inspiration to all who worked with him. He will be sorely missed not only by his family but also by a wide circle of personal friends and clinicians, including many active clinical investigators throughout the country. His name will stand out as one of the leading American men of science and allergy.

J. Warrick Thomas

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(Continued from Page 172)

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DIAGNOSIS OF HYDATID DISEASE. Bull. Lederle Lab., 11:29, (Nov.) 1943.

Hydatid disease or echinococcosis, is an infection with the larval or hydatid stage of a tapeworm, Echinococcus granulosus. It was the first parasitic infection for which diagnostic immunological tests were successful. These tests depend upon the presence of antibodies in the circulation or tissues of the patient. Precipitin, complement fixation and skin tests all have been utilized in diagnosis. Antigens from heterologous cestodes give a reliable "non-specific" postive immediate reaction in about 95 per cent of patients harboring hydatid cysts. Intradermal tests are performed with 0.01 c.c. of 1:100 tapeworm extract. Positive skin test should be interrupted with regard to history, symptoms and laboratory findings including stool examinations to rule out intestinal cestode infestations.

L. J. H.

News Items

FUNDS FOR RESEARCH IN ALLERGY

In accordance with the policy established by the College in 1942, a Research Foundation has been firmly established by the College. The College initiated the first Fund to be used for encouraging research in allergy by appealing to 100 Fellows of the College who are able and willing to do so to contribute $50 each towards the Fund and that such contributors are to constitute an Honor Roll. The voluntary response of members has been very satisfactory.

On February 28, 1944, Marcelle Cosmetics, Inc., made their first annual gift of $500 to the College to be known as the Marcelle Research Fund. The grant is to be repeated each year for a period of five years. This Fund shall be administered by whatever officers or agency the College shall designate, the money to be used in such research in the field of allergy deemed by the administrators worthy of support. Members of the College who have been selected for the administration of this Fund are nationally recognized personalities in allergy and have had extensive experience in research problems.

The College wishes to express its sincere appreciation to the Marcelle Cosmetics, Inc., for this manifestation of their confidence and high esteem in the organization, when accepting such a worthy gift.

Captain Alfred L. Seal (MC) has been retired to the inactive reserves and has opened an office in the Beverley Hills district in Los Angeles. His home address is 1844 Wooster Street, Los Angeles 25, California.

The Southwest Allergy Forum held a very satisfactory and enthusiastic two-day informal round table discussion on practical allergy subjects at Jackson, Mississippi, April 15 and 16. The program was varied, and the leaders and coördinators represented outstanding allergists of the Southwest.

The College library gratefully acknowledges reprints from many of the Fellows the past two months, including various monographs and reprints from South America. The latter include "Anemopolinologia Aplicada," by Dr. Miguel Augustin Solari, of Buenos Aires; "Las Manifestaciones Alergicas des Aparato Urinario," and "Sobre Alergia Fisica," by Dr. Mariano R. Castex, of Buenos Aires; "Alergia Polinica" Separata do Brasil, by Dr. O. Oliveira Lima, of Rio de Janeiro; "Polinosis," by Dr. Leopoldo H. Ballestero and Dr. Juan V. Monticelli, of Buenos Aires.

The College membership certificates are being mailed now, as rapidly as completed. Certificates will not be sent abroad to those in the Service since they are framed, but will be sent to the home address. Those members abroad who do not have a home address at present will have their certificates held until further instructions are received from them.

The College is very grateful to Almay, Inc., New York, for furnishing the cocktail hour preceding the informal dinner of the Annual Meeting, Saturday evening, June 10, Palmer House, Chicago.

AUSTRALIA

Dr. Bernard Riley, Harley, 143 Macquarie St., Sydney, N.S.W., Australia, has qualified as an Active Fellow of the College. Dr. Riley is Medical Officer, in charge of the Allergy Clinic of the Royal North Shore Hospital of Sydney.

BOOK REVIEW

THE 1943 YEARBOOK OF DERMATOLOGY AND SYPHILOLOGY. Edited by Marion B. Sulzberger, M.D., and Rudolph L. Baer, M.D., 584 pages, 72 illustrations. Price—$3.00. Chicago: The Year Book Publishers, 1943.

Dr. Fred Wise, former editor of the Year Book of Dermatology and Syphilology, has retired from this position to be succeeded by his co-editor Dr. Marion B. Sulzberger (Comdr. MC, USNR). Dr. Sulzberger has chosen Dr. Rudolf L. Baer as his assistant editor. In line with rulings by the War Productions Board, the publishers have introduced the volume with a lighter weight paper, printing more words to the page and reducing the margins. The result is a very compact, durably bound, easily read volume, without sacrificing any of the contents.

Dr. Sulzberger, also noted for his clear concise expression, admirably succeeds in following the precepts of Dr. Wise. The editor recognizes the proper importance of the role of immunology and allergy in dermatologic diseases. However, the entire range of skin diseases, based upon recent authoritative literature, is adequately presented with our present-day knowledge of their recognition and management.

A very complete practical guide for skin tests and other immunologic procedures in common dermatologic and venereal diseases is given in the opening chapter. Throughout the book cutaneous hypersensitivities to topical applications and internal medication are stressed. The therapy of nonvenereal diseases and x-ray and other physical therapy are discussed in detail. Eczema, urticaria and allergy; the hematogenous dermatoses; miscellaneous dermatoses; fungous and other infection of the skin; tumors; venereal diseases and therapy, together with a chapter on investigative studies, are completely presented.

The omission of nonessentials makes the book a compact manual of skin diseases which every practitioner should always have at hand. —F.W.W.

Attention Please!

IMPORTANT NOTICE

Hotel and traveling reservations for the Annual Meeting should be made NOW.

Consult map of Chicago loop district convention hotels, pages 132-133, for details.

Also see convention number, *Journal of the American Medical Association.*

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*"A new type of medication to be used in Bronchial Asthma and other Allergic conditions." New Eng. Jour. of Med., 223:843-846, 1940.

Literature Upon Request

BREWER & COMPANY, Inc., Worcester, Mass.